Archives of Dermatology and Syphilology

VOLUME 48 OCTOBER 1943 NUMBER 4

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MYCOSIS FUNGOIDES WITH BULLOUS LESIONS

REPORT OF A CASE RESISTANT TO ROENTGEN AND ARSENICAL THERAPY; EFFECTS OF EMPIRIC THERAPY, PARTLY BASED ON LABORATORY INVESTIGATIONS

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Bullous and vesicular lesions are occasionally encountered as intrinsic elements in such eruptions as lichen planus, leprosy and (more rarely) lupus erythematosus. As a conspicuous manifestation of eruptions of mycosis fungoides, they are extremely rare. Bullous and vesicular lesions sometimes become manifest as a result of interference with the circulation of lymph, giving rise to "wet" lesions of secondary nature, in contradistinction to the primary and essentially "dry" lesions. For example, bullous lesions occurring in association with Kaposi's idiopathic hemorrhagic sarcoma—a dry eruption—have been described[1]; these are secondary elements caused by blockage of the flow of lymph.

In the patient forming the subject of this report, the bullous lesions not only appeared at the site of clinically normal skin but arose—for the most part—from the midst of infiltrated nodules and plaques. Thus, the eruption was mistaken for pemphigus by several experienced dermatologists.

The evolution and involution of such bullous elements, starting from an infiltrated nodule or flat plaque, increasing from vesicle to bulla, bursting, forming an adherent crust and then regressing, was observed over a period of several months. They contained serum, not lymph.

In view of the fact that treatment of this patient with roentgen rays and arsenic proved futile, it was decided that a trial of various empiric remedies, the rationale of which was based in part on extensive laboratory investigations, was justified.

REPORT OF A CASE

History.—D. K.,[2] a man aged 67, applied for treatment at the skin and cancer unit of the New York Post-Graduate Medical School and Hospital on Dec. 14, 1939, presenting generalized cutaneous lesions of two years' duration. His mother died of "cancer of the stomach" at 23 years and his father of pneumonia at 63. One brother died of "cancer of the intestines" at the age of 50 and another of "diabetes." He has six brothers and one sister living and well and six "healthy" children. He stated that he had not taken any medicaments as laxatives or for colds or other ailments. He had a pea-sized penile blister when he was 18. He was hospitalized in South Africa in 1902 for two weeks for "dysentery." Since then he

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1. Wise, F., and Eller, J. J.: Bullous Eruptions in Hemorrhagic Sarcoma of Kaposi and in Lichen Planus, Arch. Dermat. & Syph. **7**:625 (May) 1923.

2. The patient was presented before the New York Dermatological Society March 24, 1942 (Wise, F.: Mycosis Fungoides with Bullous Lesions, Arch. Dermat. & Syph. **46**:773 [Nov.] 1942).

had been in "perfect health" until the onset of the eruption. He has been a tailor for fifty years but has limited himself for the past ten years to pressing dry-cleaned clothes.

A pedunculated almond-sized growth was removed in 1937 from the middle of the back. This area later began to itch. Circumscribed erythematous dry and nonscaly patches gradually developed within two years on the abdomen, thighs and legs. These became pruritic when he perspired and when he was "heated up." Examination on Dec. 14, 1939 revealed yellowish brown mottled areas scattered over the chest, abdomen and thighs and discoid nummular, infiltrated plaques on the thighs and legs. The clinical diagnosis was "dermatitis." The histologic interpretation of a lesion of the right thigh was "superficial dermatitis, not characteristic of any clinical entity." He was treated with antipruritic emollient lotions and with weekly generalized exposures to a quartz mercury vapor lamp.

Fig. 1.—Photograph showing the bullae on the lower part of the back arising from the plaques and superficial patches. The numerous seborrheic verrucae are clearly seen.

The patient returned to the clinic on Feb. 18, 1941, complaining of the spreading of the eruption and severe itching. The lesions at that time revealed the clinical features of mycosis fungoides. He stated that in January 1940 red spots or blotches, "like a solution spread out on the skin," made their appearance on the inner surfaces of the thighs and legs. Similar lesions developed on the scalp eight months later, and then the sides of the neck, the shoulders and the front of the chest became successively affected. Some patches seemed to vanish after a varying period, while new ones appeared in the adjacent areas. Other patches were persistent, rose above the surface of the skin and later became rough and flaky. On Feb. 4,

1941, blisters developed on the scalp, face, back of the neck and upper part of the back. These blisters burst by themselves or on slight irritation. The fluid was "brownish, sticking like mucilage." The blisters on the trunk were painful but not those on the head. They occurred mostly in the summer and less frequently in the winter.

Dermatologic Examination (Feb. 18, 1941).—The lesions were generalized, excepting on the palms and soles, and were multiform and symmetric. They consisted of thin-walled, clear vesicles and bullae, some distended and some flaccid and ruptured, of plaques and of superficial discoid patches. The intervening areas appeared normal. All surfaces were involved, especially the flexor surfaces. The entire scalp was studded with pea-sized to almond-sized hemorrhagic raw and crusted areas.

At the beginning the vesicles and bullae appeared on the scalp, face, neck and upper part of the back. Since January 1942 they have also been erupting on the trunk and limbs. Most of the bullae developed in the center of the plaques and superficial patches (fig. 1). They varied in size from that of a pea to that of a cherry and occasionally were even as

Fig. 2.—Photograph showing the large egg-sized bullous lesion on the upper part of the back, which responded partially to ½ unit of superficial roentgen rays (150 r).

large as a small egg (fig. 2). They contained clear fluid and were fairly firm at first, later collapsing and rupturing, leaving raw, denuded areas, some of which were hemorrhagic.

The nonbullous lesions consisted of well marginated pea-sized to egg-sized, discrete and confluent, nonscaly, smooth and erythematous superficial patches; of solid dull red, rough, nummular, padlike indurated plaques covered with adherent furfuraceous scales and of large superficial, less clearly defined crescentic and irregular areas disseminated over the entire trunk and limbs. Some of the superficial patches had central clearing and faded partially on diascopic pressure, while the nummular plaques were not at all modified by it. On the back (fig. 1) were numerous seborrheic keratoses. The buccal mucosa was studded with papules of Fordyce's disease. There was a pronounced granular pharyngitis. There were no palpably enlarged lymph nodes.

General Physical and Special Examinations.—The patient was a plethoric and obese man, in apparent good health, 5 feet 6 inches (165 cm.) in height and 185 pounds (84 Kg.) in weight. The blood pressure was 130 systolic and 70 diastolic in the right arm and 110 systolic and 60 diastolic in the left arm. The heart sounds were of good quality. The lungs were clear. The abdomen was soft and protuberant. There was no odor emanating from the lesions.

The Nikolsky sign could be elicited in the affected areas but not in the normal-appearing integument.

The pupils were small and irregular, the right somewhat larger than the left. They reacted poorly to light and in accommodation. Examinations of the peripheral fields done by Dr. Charles N. Romaine on Aug. 22 and Sept. 3, 1942 showed a moderate contraction of the visual fields. The electroencephalogram interpreted by Dr. Bernard L. Pacella did not reveal any abnormal electrocortical activity.

A roentgenogram of the chest revealed a "moderately enlarged aortic type heart, a moderate old hilus and root branch thickening, with probable puerile type central lymphoid deposits." Examination of the skull showed "no abnormality in detail or outline of the bones of the vault or base."

Laboratory Data.—The urine was normal on several examinations except for traces of albumin. The Mosenthal test and the examinations for urobilin and bile pigment gave negative results. A quantitative analysis of a twenty-four hour sample of urine yielded the following values: volume, 900 cc.; phosphorus, 2.1 Gm., as phosphorus pentoxide (P_2O_5) (normal 2.5 to 3.0 Gm.), and protein, 0.018 Gm., per hundred cubic centimeters. Several hemograms were normal except for 12 per cent band neutrophils on Feb. 18, 1941 and 14 per cent eosinophils on Sept. 13, 1942. The chemical examination of the blood on Feb. 20, 1941 revealed normal values except for 23.5 mg. of urea nitrogen (normal 10 to 15 mg.), 5.2 mg. of uric

Bone Marrow Smear *

Type of Cell	Percentage	
	Normal	Observed
Myelocyte series, 44.5 per cent		
Polymorphonuclear neutrophils	24 to 30	15
Polymorphonuclear eosinophils	1	5
Polymorphonuclear basophils	..	0.5
Metamyelocytic neutrophils	10 to 15	8
Metamyelocytic eosinophils	10 to 15	2
Myelocytic neutrophils	30 to 40	9
Myelocytic eosinophils	30 to 40	2
Promyelocytes	1	1
Myeloblasts	..	1
Hemohistioblasts	1	1
Monocytes	2	5
Large lymphocytes	8	3
Lymphocytes	6	8
Nucleated red cells		
Megaloblasts	2 }	3
Macroblasts	2 to 5 } 15 to 20	11
Normoblasts	12 to 15 }	22
Plasmocytes	1	3
Mitotic figures	..	0.5
		100

* Five hundred cells were counted.

acid (normal 2 to 4 mg.) and 410 mg. of chlorides as sodium chloride (normal 450 to 500 mg.) per hundred cubic centimeters of blood. The Mantoux tuberculin test gave a negative reaction with a dilution of 1:10,000 but elicited a 2 plus response with a concentration of 1:5,000. Patch tests made on active, clearing and unaffected areas of the chest gave negative reactions to 20 per cent and a positive response to 40 per cent of potassium iodide test ointments. Cultures from the lesions for bacteria yielded Staphylococcus aureus and Bacterium coli commune. Examination of a smear from the fluid of an unruptured bulla gave the following cell count: polymorphonuclear neutrophils 54 per cent, lymphocytes 24 per cent and monocytes and eosinophils 11 per cent each. The eosinophil count rose to 35 per cent on Aug. 21, 1942. The Pels-Macht phytopharmacologic test gave a reading of 38 per cent (normal 70 to 75 per cent). The sedimentation rate was 15 mm. per hour on Sept. 2, 1941 and 40 mm. per hour on Oct. 6, 1942 (normal 10 mm. in a male, by the Westergren method).

Sternal Puncture.—A sternal puncture was made on Sept. 12, 1942. The bone marrow smears examined by Dr. N. M. Richter showed a large number of red cells and a slight increase in eosinophils and plasma cells.

The detailed report of the sternal puncture[3] count in tabular form was given by the former resident of the Post-Graduate Hospital, Dr. George Leclerc, who made special studies in this field.

3. Weil, P. E., and Perles, S.: La ponction sternali, procédé de diagnostic cytologique, Paris, Masson & Cie, 1938.

Interpretation of Sternal Marrow Count.—"The differential count of the bone marrow is within normal limits except for the high proportion of nucleated red cells (36 per cent), for the moderate eosinophilia (9 per cent) and for the presence of plasmocytes.

"The cells of the myelocytic series have an absolutely normal appearance. Their number is decreased (44.5 per cent) because of the high percentage of the nucleated red cells. Their maturation occurs normally, as shown by the relative number of myelocytes, metamyelocytes and polymorphonuclear neutrophils. A moderate increase in eosinophils in the bone marrow is frequently found in patients with chronic cutaneous diseases. A count of 5 per cent monocytes in bone marrow is somewhat high.

"The nucleated red cells are definitely increased, especially the younger cells represented by the megaloblasts and macroblasts. This is an unexpected observation in mycosis fungoides. It may be due to the large number of injections of sodium arsenate the patient received, which inhibited to a certain degree the maturation of the red cells. A plasmocyte count of 3 per cent is a definite elevation above the normal. There is absolutely no evidence of leukemia of any type.

"Conclusion: The bone marrow is normal with a greatly increased number of erythrocytes, a moderately increased number of eosinophils and a slightly increased number of plasmocytes."

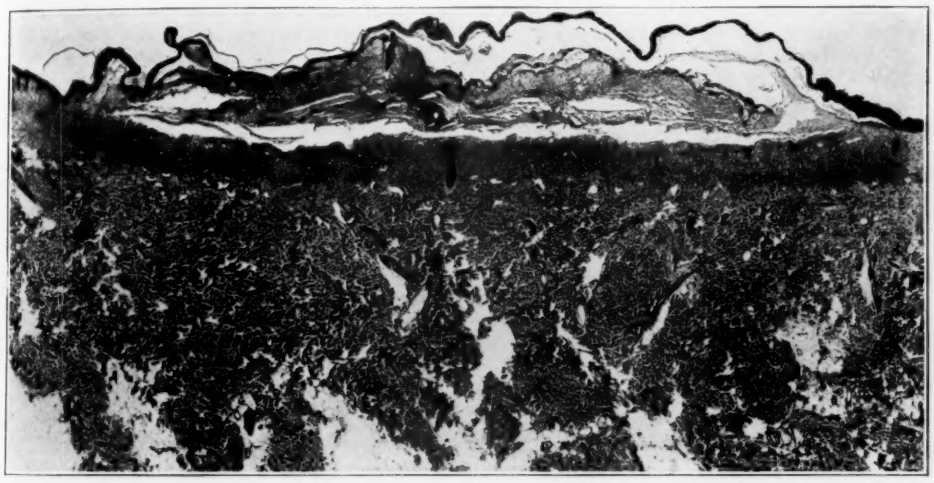

Fig. 3.—Photomicrograph showing an unbroken bulla arising from a mycosis fungoides lesion (× 14).

Histologic Observations.—A section taken on Feb. 20, 1941 from a nonbullous infiltrated plaque in the right thigh was examined and interpreted by Drs. Satenstein and Sachs. The observations were summarized as follows: "The reticulum, the polymorphic cellular infiltration, the mitoses and Pautrier's abscesses are all in favor of a diagnosis of mycosis fungoides."

Our next problem was to establish the diagnosis of mycosis fungoides on a bullous lesion. Several biopsies were made at different intervals until we obtained on Feb. 19, 1942 a good section of a bulla arising from the interior of an infiltrated plaque. On the histologic structure of that section (demonstrated by Dr. Wise before the New York Dermatological Society [2]) the diagnosis of mycosis fungoides with bullous lesions was established. Another biopsy specimen was taken on Sept. 7, 1942. This section (fig. 3) showed the histologic structure of mycosis fungoides still more clearly than the aforementioned one. It was examined by Dr. J. Frank Fraser, Dr. Hamilton Montgomery and Dr. Wilbert Sachs. Dr. Fraser stated that the section showed "epidermal vesicles and a polymorphous infiltrate in the upper layers of the corium composed of lymphocytes, polymorphonuclear leukocytes, eosinophils and reticulum cells. This histologic picture is consistent with the diagnosis of bullous mycosis fungoides." Dr. Montgomery examined these sections and confirmed the diagnosis of mycosis fungoides.

Dr. Sachs described the changes (fig. 3) as follows: "Extending throughout the upper part of the cutis and up to the epidermis is a broad bandlike cellular infiltration. At one

point there is a large subepidermic bullous formation. The overlying epidermis is thin but otherwise shows no important change. The cellular infiltration is composed of small round cells, wandering connective tissue cells, plasma cells, eosinophils and many epithelioid cells. There are several multinuclear plasma cells (Marschalko cells). Between the cellular elements is a fine reticulum. There is some grouping of the cells and an occasional mitotic figure. There are no Pautrier abscesses in this section. The features described are sufficient to permit a diagnosis of mycosis fungoides."

Treatment.—Between March 25 and Aug. 25, 1941, the patient was treated with roentgen rays and arsenical medication. Five weekly superficial exposures to roentgen rays of 75 r each were given to the affected areas. Solution of potassium arsenite (Fowler's) in daily increasing doses was taken per os until 20 drops three times a day was reached. Two per cent solution of sodium arsenate was injected simultaneously in increased daily doses beginning with 3 minims and ending with 28 minims (1.7 cc.) per day. The arsenical therapy was then discontinued because of complaints of gastrointestinal distress, dizziness and garlic-like taste. There was no improvement from these treatments.

On Sept. 2, 1941 an injection of 1 cc. of alum-precipitated diphtheria toxoid was given subcutaneously in the left arm. A week later the patient felt much better and complained of only slight itching. Most of the bullous lesions on the scalp and face showed signs of regression and healing. The plaques on the body were paler and smaller. New blisters did not appear. On September 13 there was further improvement. The discoid lesions were covered with fine scales. On September 23 regression was still more pronounced. The scalp was almost healed. A second injection was then given. On October 3 he received the third and on October 12 the fourth injection of diphtheria toxoid, 0.5 cc. each. On the latter date the improvement was more evident, most of the bullous lesions on the back having dried.

Because of the apparently good response, the patient was presented before the Manhattan Dermatologic Society on Oct. 14, 1941 [4] and his case considered as 1 of 4 cases of various dermatoses treated empirically with diphtheria toxoid therapy.

The benefit resulting from the diphtheria toxoid lasted from September 9 till November 2. The nonbullous lesions showed a decided change as revealed by the complete resolution of some of them while others became more flattened and less infiltrated. The bullous lesions, however, continued to sprout out anew.

From Nov. 10, 1941 till Aug. 25, 1942 the patient was treated experimentally with the following remedies: Calcium pantothenate 1 tablet (10 mg.) three times daily until 200 tablets were taken. On Nov. 14, 1941 6 minims (0.37 cc.) of desoxycorticosterone acetate solution [5] was administered by sublingual instillation three times daily. This dose was doubled on December 28 (this being equivalent to 6 mg. and 12 mg. daily respectively of the hormone given by mouth). From November 24 for three weeks 1 cc. of aqueous extract of orchic tissue was injected subcutaneously twice weekly. On Jan. 4, 1942 1 tablet of sulfadiazine (2-[paraaminobenzenesulfonamido]-pyrimidine), 0.5 Gm. each, with 2 Gm. of sodium bicarbonate to a glass of water was prescribed to be taken three times daily. From Jan. 16 till July 21, 1942, nine superficial roentgen exposures, a total of 1 unit, 300 r, was given to each of the various affected areas of the body.

These varied treatments gave the patient only temporary relief and clinical improvement. He was therefore hospitalized at the Post-Graduate Hospital on August 3, with the view of observing him more closely and possibly rendering more effective treatments.

Treatment with injections of arsenic was again used but proved to be of no benefit. Ten per cent sulfathiazole ointment was applied locally. Chloral hydrate in 1.4 Gm. doses was given for insomnia. Starch baths were taken daily. On August 12, 150 mg. of vitamin C, and on August 22, 300 mg., was given daily. These treatments proved ineffective. Numerous bullae continued to develop constantly. There were many exudative lesions on the back. It was then decided to treat the patient experimentally with androgen therapy. Testosterone propionate was given intramuscularly on September 24, and its use was continued for twelve consecutive days in 10 mg. doses. Two days later improvement was already noticeable. On October 8 he was discharged as improved.

After his discharge from the hospital the patient received two injections of testosterone propionate of 25 mg. each per week for six weeks. He was also taking concurrently 2 tablets a day of methyl testosterone, 10 mg. each. Ascorbic acid in tablet form was later pre-

4. Wise, F.: A Case for Diagnosis (Mycosis Fungoides?), Arch. Dermat. & Syph. **45**: 285 (April) 1942.

5. Desoxycorticosterone acetate in propylene glycol with 20 per cent alcohol (10 mg. per cubic centimeter).

scribed in doses of 1 Gm. a day for ten days and 0.5 Gm. a day for ten more days and then continued in doses of 0.3 Gm. a day.

With this regimen the patient continued to improve. He felt more cheerful and hopeful, in contrast to his previous depressed state and concern about his illness. Only an occasional bulla appeared. The affected areas, especially of the upper part of the back, which were previously soft, hemorrhagic and mushy, were now firm and smooth and almost cleared, except for small superficial erosions. The face was also much improved.

On December 29 the patient complained of dizzy spells and weakness. The blood pressure was 130 systolic and 60 diastolic in the right and 110 systolic and 50 diastolic in the left arm. The heart sounds were fainter and of poorer tone and quality than on previous examinations. The androgen therapy was therefore stopped temporarily, and instead parathyroid tablets, 0.006 Gm. each, to be taken three times daily, were prescribed. Calcium gluconate in 4 Gm. doses was ordered to be taken morning and evening with a glass of milk. This therapy was continued for one month only, as it produced no apparent change in the eruption during the month of the discontinuance of the testosterone propionate therapy.

On Feb. 7, 1943 the patient was readmitted to the Post-Graduate Hospital for the purpose of taking the tests of Robinson and co-workers.[6] It is worth quoting the entry notes made on the chart by Dr. Leclerc at the time of the patient's admittance to the hospital:

"Feb. 10, 1943: The patient is much better than he was at the time of his last discharge. There are now no bullae. The whole back shows lichenification, erythema and scaling. The upper part of the back shows some erosive areas of various sizes, up to about 1 cm. in diameter. There is slight crusting of the upper area of the back. Scattered over the whole body are large and small erythematous scaly plaques, some with, most of them without, infiltration. Some show pigmentation of light brown color. The scalp is at present almost clear of lesions. There are very few lesions in the face."

Since March 11, 1943 the patient has again been treated with injections of testosterone propionate, 25 mg. each, twice weekly. The vitamin C therapy is being continued in the form of 100 mg. tablets of ascorbic acid three times daily, in combination with enteric-coated tablets of desiccated anterior pituitary substance[7] of 0.3 Gm. each, three times daily.

An interesting occurrence has been the gradual but steady disappearance of most of the numerous seborrheic verrucae which studded the upper two thirds of the back. This was first observed three weeks after the administration of testosterone propionate. The previous roentgen therapy seemed to have had no effect on these nevoid seborrheic keratoses.

COMMENT

Review of the Literature.—The occurrence of bullous lesions in mycosis fungoides has occasionally been reported in the literature. Ormsby[8] stated that in the premycotic stage vesicles or bullae are occasionally present and that he had seen patients with mycosis fungoides who had annular lesions, some vesicular or bullous.[9] A woman with generalized mycosis fungoides was presented at a meeting by O'Leary, Montgomery and Brunsting.[10] She had a few small bullae on the abdomen. Wile[11] presented a 69 year old man with mycosis fungoides who had one bulla on the wrist and who at one time had bullae on the corneas. Wile and Knerler[12] reported the occurrence of mycosis fungoides in a mother and daughter. The daughter had vesiculation of the palms and soles, which eruption

6. The results of these tests together with the discussion of the laboratory data dealing with renal and adrenal insufficiency are the subject of another paper concurrently being sent for publication.

7. Each grain (0.06 Gm.) of the desiccated product represents 5 grains (0.3 Gm.) of fresh gland substance.

8. Ormsby, O. S.: Disease of the Skin, ed. 4, Philadelphia, Lea & Febiger, 1934, p. 904.

9. Ormsby, O. S., in discussion on Wile, U. J.: Mycosis Fungoides, Arch. Dermat. & Syph. **36**:903 (Oct.) 1937.

10. O'Leary, P., in discussion on O'Leary, P. A.; Montgomery, H., and Brunsting, L. A.: Mycosis Fungoides, Arch. Dermat. & Syph. **31**:406 (March) 1935.

11. Belote, G. H., in discussion on Wile, U. J.: Mycosis Fungoides, Arch. Dermat. & Syph. **33**:387 (Feb.) 1936.

12. Wile, U. J., and Knerler, C. W.: Mycosis Fungoides in Mother and Daughter, Arch. Dermat. & Syph. **38**:939 (Dec.) 1938.

later became widespread and involved the face and neck. Lortat-Jacob [13] mentioned a case of mycosis fungoides "with bullous ulcerative elements of cyclic or polycyclic arrangement" in a man aged 36. It is recorded in Jadassohn's [14] posthumous work that rarely bullae similar to those in pemphigus and dermatitis herpetiformis occur in mycosis fungoides.

It is not clearly stated in the reports of any of the aforementioned cases (except by Ormsby [9]) that the bullae arose from the infiltrated lesions of mycosis fungoides themselves. It may then justifiably be assumed that the bullae were independent lesions and did not arise from the active plaques and patches. We could not find any histologic descriptions or photomicrographs showing, as in our case, the presence of bullae arising from the lesions of mycosis fungoides. The designation mycosis fungoides bullosa is suggested as being applicable to our case in preference to mycosis fungoides with bullous lesions, in analogy to lichen planus bullosus, lupus erythematosus bullosus and erythema multiforme bullosum.

Differential Diagnosis.—The patient was presented at several dermatologic meetings. The diagnoses of pemphigus vulgaris, a drug eruption, erythema multiforme and pemphigus erythematosus (Senear-Usher syndrome) were entertained. Only the diagnosis of pemphigus vulgaris was seriously considered by several dermatologists. Clinically pemphigus was later ruled out by the appearance of multiform plaques characteristic of mycosis fungoides, by the development of most of the bullae from the plaques and superficial patches and by the patient's continuous good health. The diagnosis was later confirmed by supplementary histologic sections.

Discussion of Treatment.—Arsenic has been one of the standard accepted remedies for mycosis fungoides. However, in this case and 3 other cases of mycosis fungoides in which the patients were treated by us with injections of 2 per cent sodium arsenate solution there was no benefit either in relieving the itching or in resolving the lesions. We have since been prescribing, wherever arsenic therapy is indicated, arsenous acid in the form of so-called asiatic pills, each containing $\frac{1}{16}$ grain (0.0038 Gm.) of arsenic. One pill three times daily at first, with a gradually increased dose, is usually ordered. It will require time to evaluate the therapeutic value of this medication as compared with that of injections of sodium arsenate.

Superficial roentgen treatment gave only temporary relief. The immediate beneficial effect of $\frac{1}{2}$ unit (150 r) of roentgen rays was observed on the egg-sized fungating bullous lesion on the upper part of the back. Within a week it flattened and showed signs of healing. However, continuation of the roentgen treatment failed to heal the bullae completely, and new bullous lesions continued to appear.

The idea of using injections of orchic extract simultaneously with diphtheria toxoid was based on the theory of the "spreading factor" advanced by Duran Reynals.[15] This author found that testicular extract enhanced greatly the lesions produced by intradermal inoculation of vaccine virus. We thought that orchic extract might similarly enhance the antitoxic action of diphtheria toxoid. How-

13. Lortat-Jacob and Legrain, B.: Mycosis Fungoides with Bullous, Ulcerative Elements, of Cyclic or Polycyclic Arrangement, Bull. Soc. franç. de dermat. et syph. **33**:623, 1926; abstracted, Arch. Dermat. & Syph. **15**:341 (March) 1927.

14. Jadassohn, J.: Dermatologie, Berne, Switzerland, Weidmann & Co., 1938, pp. 498-502.

15. Duran Reynals, F.: Increase of the Activity of Vaccine Virus by the Extracts of Certain Organs, Compt. rend. Soc. de biol. **99**:6 (June) 1928.

ever, this extract was not given in sufficient quantities and for a long enough period to make possible an evaluation of its usefulness.

Three tablets of sulfadiazine of 0.5 Gm. each given daily for several weeks prior to the patient's admittance to the hospital and 5 per cent sulfadiazine ointment applied to the lesions during his stay in the hospital failed to show any appreciable beneficial changes in the bullous lesions.

Desoxycorticosterone acetate was ordered on the basis of probable adrenal insufficiency.[16] Calcium pantothenate was given concurrently with the desoxycorticosterone on the theory that in adrenal insufficiency there may be a lack of pantothenic acid, since deficiency of this hormone has been reported to be associated with hemorrhages in the adrenals in rats.[17] No appreciable improvement was noticed from the use of these substances.

The remarkably rapid effect of testosterone propionate, shown by the noticeable regression of the bullae within a few days, may be the result of its direct beneficial action on the adrenals and the kidneys. It has been already established that the androgens are chemically related and exhibit some of the metabolic effects of the hormones of the adrenal cortex. They cause a retention of the extracellular electrolytes and fluid and a diminution in the excretion of nitrogen, potassium and inorganic phosphorus.[18] Selye[19] observed that the injection of testosterone caused a notable enlargement of the kidneys in experimental animals and rendered them less susceptible to toxic agents.

Vitamin C was given concurrently with the testosterone propionate because of the definite vitamin C deficiency in the blood, the greater requirement for vitamin C in infections and wound healing, the findings of Giroud and co-workers[20] and the observations by Liffschitz[21] that vitamin C combined with adrenal cortical extract has a stimulating effect on bacteriolysis and antibody formation in infections. Since there is a chemical relationship between the androgens and cortical hormone, vitamin C may have an effect (synergistic?) on testosterone propionate similar to the possible effect of this vitamin on the cortical hormone.

The rationale of giving anterior pituitary substance is based on the experimental findings of Evans[22] that anterior pituitary extracts caused repair of atrophied adrenal cortex.

An interesting occurrence has been the gradual but steady disappearance of most of the numerous seborrheic verrucae which practically covered the upper two thirds of the back in our patient. This effect was first observed three weeks after the administration of the testosterone propionate. This could not be attributed to the denudation of the skin caused by the rupture of the bullae, as only a small portion of the back has been affected by the bullous lesions and no diminu-

16. Adrenal insufficiency was suspected by the authors before the tests which pointed to pathologic changes in the adrenal glands were performed.[6]

17. Daft, F. S.; Sebrell, W. H.; Babcock, S. H., Jr., and Jukes, T. H.: Effect of Synthetic Pantothenic Acid on Adrenal Hemorrhage, Atrophy and Necrosis in Rats, Pub. Health Rep. **55**:1333 (July 26) 1940.

18. Goodman, L., and Gilman, A.: The Pharmacological Basis of Therapeutics, New York, The Macmillan Company, 1940, p. 1210.

19. Selye, H.: The Effect of Testosterone on the Kidney, J. Urol. **42**:637 (Oct.) 1939; cited by Goodman and Gilman.[18]

20. Giroud, A.: Santa, N.; Martinet, M., and Bellon, M. T.: Function of Ascorbic Acid in Secretion of Hormones of Adrenal Cortex, Bull. Soc. chim. biol. **23**:108, 1941.

21. Liffschitz, L.: Algunas consideraciones sobre la relación entre la vitamina C y la corteza de suprarrenal, Semana méd. **2**:643 (Sept. 15) 1938.

22. Evans, cited by Harrop, G. A., in Tice, F.: Practice of Medicine, Hagerstown, Md., W. F. Prior Company, Inc., 1921, vol. 8, p. 307.

tion in these growths has been observed before the injections of this hormone. The superficial roentgen exposures, the last of which was given nine weeks previously, did not seem to have any effect on these nevoid growths. The dilating effect of testosterone on the blood vessels [23] may be a factor responsible for the falling off of the seborrheic verrucae.

SUMMARY

It is suggested that "bullosa" be added to "mycosis fungoides" to describe the disease in our case, as in such terms as "lichen planus bullosus" and "erythema multiforme bullosum," because of the development of the bullae from the mycosis fungoides lesions.

Arsenic in the form of injections of sodium arsenate and superficial exposures to roentgen rays gave only partial and temporary relief. Sulfadiazine given per os and sulfathiazole in 10 per cent ointment, desoxycorticosterone acetate administered by sublingual instillation, pantothenic acid tablets and vitamin C did not improve the eruption. Alum-precipitated diphtheria toxoid cleared up the lesions almost completely for several weeks, but the bullae later recurred.

Testosterone propionate given at first in 10 mg. doses for twelve consecutive days produced noticeable improvement within a week.

An unusual occurrence has been the steady disappearance of the numerous seborrheic verrucae from the back. The authors are now using this hormone experimentally for similar nevoid dermatoses.

The Abbott Laboratories supplied the pantothenic acid, and the Schering Corporation supplied the desoxycorticosterone acetate.

Drs. Charles F. Sims and Max Jessner aided in interpreting the histologic observations, and Mrs. Etnah Rochon Boutte, supervisor of the social service department, assisted in performing the various tests and examinations.

Mrs. Eleanor Moreland, of the photographic department, prepared the photographs and photomicrographs.

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23. Walker, T. C.: Use of Testosterone Propionate and Estrogenic Substances in Treatment of Essential Hypertension, Angina Pectoris and Peripheral Vascular Disease, J. Clin. Endocrinol. **2**:560 (Sept.) 1942.

CALAMINE AND NEOCALAMINE, 1942

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The appearance of the official Pharmacopeia of the United States XII, and the National Formulary VII (November 1942) warrants the presentation of a few items of interest to dermatologists.

The description of calamine and neocalamine from the official texts should remove for all time the ancient ideas regarding the character of these preparations. The early texts gave less simple definitions for the calamine of the pharmacy. Prior to 1914, there may have been some form of calamine available with special chemical characteristics. But the description of prepared calamine as "calcined zinc carbonate" really meant zinc oxide, for the process of calcining drove off the carbon dioxide and left the oxide form of the zinc. Whether calamine (prepared) or neocalamine (prepared) is utilized, the only ingredient is zinc oxide slightly and variously colored with some form of iron rust. The color of the neocalamine is a closer match to that of most white skins than is the atrocious tint of calamine.

The inclusion of magma of bentonite serves an excellent purpose. It permits of uniformity of sampling. The calamine lotion always had the unhappy tendency of changing with each application, because too much of the powder adhered to the sides of the container. Also to be noted is that the superstition of humoral pathology reflected in the mild alkaline solution of calcium hydroxide is forgotten in the lotion of prepared neocalamine. The glycerin also is omitted.

Dermatologists who prescribe prepared neocalamine and the magma of bentonite should request the pharmacists in their localities to stock the necessary ingredients. They may also enjoy the exercise of actually experimenting in the preparation of these formulas, and in the exacting study of color matching for individual patients.

The formulas in the "National Formulary" and in the "Pharmacopeia of the United States" are easily available to physicians.

A method of improving the sample of the lotion applied to the skin may be tested. A neutral soap suspension of stearic acid and triethanolamine is an excellent vehicle for the prepared calamine and the prepared neocalamine. The powders settle slowly if at all.

SUGGESTED FORMULA FOR SUSPENSION OF COLORED ZINC OXIDE (CALAMINE OR NEOCALAMINE)

	Gm. or Cc.
Stearic acid	4
Triethanolamine	1
Water, enough to make	100
To which add	
(*a*)	
Prepared calamine	8
Zinc oxide	8
or (*b*)	
Prepared neocalamine	15
or (*c*)	
Prepared neocalamine	8
Zinc oxide	4

18 East Eighty-Ninth Street.

TREATMENT OF SCABIES IN WARTIME

MAURICE OPPENHEIM, M.D.
AND
HENRY A. SMITH, M.D.
CHICAGO

Scabies increases in wartime, as every physician knows and as history shows. One may expect in this global war a heavy increase in scabies. Even now the spread is observable. In an outpatient department of a medical school admitting on an average 500 patients a year there were only 7 cases in three years; in the year 1942 there were 9 cases. This is an indication of the increase to be expected among the civilian population.

As a major in World War I and after the war as chief of the dermatologic department at the Wilhelminenspital, Vienna, one of us (M. O.) observed the incidence of scabies from the beginning of the war until its end and afterward among the civilian population and devised a method for the rapid cure of the disease.

In the Wilhelminenspital there were 18 cases in January 1915, 33 in January 1916, 101 in January 1917 and 125 in January 1918.[1] This is a sevenfold increase.

It was not only the poorer classes of the population who were affected but also the middle and upper classes. Infants and small children had the disease. In some villages and towns almost the whole population was infested, and serious forms, such as Norwegian scabies, could be observed. This enormous increase was due to the general want of soap, linen and facilities for bathing and to the unclean living conditions of the front lines. Bad hygienic conditions in the homes —the overcrowded rooms and the lack of cleanliness—contributed to the spread of the disease.

The treatment previously used in Austria, the Wilkinson method for civilians and the application of betanaphthol or styrax ointment in the army, were not efficient; it took time, required absence from the daily occupation and was fairly expensive.

Equally unsatisfactory were the parasiticides used in other countries: phenol, salicylic acid and precipitated sulfur in petrolatum (Sutton); solution of sodium thiosulfate (Demyanovitch); benzyl benzoate (Nielsen, Kissmeyer); derris root; sulfur, peruvian balsam, prepared chalk and green soap in petrolatum (Pusey); Danish ointment (Sherwell, Knowles, Greenwood); pyrethrum ointment; rotenone (Epstein); potassium permanganate; solution of sulfurated lime (Vlemingkx's solution); Kleczany's oil; oil of anise, and various proprietary medicaments. All of these are useful in peacetime, when scabies has no endemic or epidemic character. They are insufficient in wartime.

A method of treatment was needed which would be effective; would take only a short time; would require no absence from duty, military or civilian; would be sure; could be applied to many persons at the same time (soldiers, school children, orphans and prisoners); would not be irritating, and would not be too expensive. After a consideration of the old French quick treatments, the Hardy method was

1. Oppenheim, M.: Die Krätzeplage und ihre Bekämpfung, Wien. med. Wchnschr. **68**:637, 1918.

chosen as the best. This was modified according to modern principles, and it gave the best results both in the army and among the civilian population.[2] From the fall of 1918 to the fall of 1922, 63,597 persons with scabies were treated in the department of cutaneous and venereal diseases at the Wilhelminenspital.

This quick method was carried out in a separate building erected for the purpose, in which more than 100 persons could be cared for each day. The following tabulation shows the number of persons treated in the period 1918 to 1922:

Year	Patients with Scabies	Patients Treated by Means of Quick Method	Patients Treated by Other Methods (Chiefly the Wilkinson)
1918-1919	14,676	11,078	3,598
1919-1920	21,697	11,976	9,721
1920-1921	18,222	11,589	6,533
1921-1922	9,002	6,711	2,291
	63,597	41,354	22,243

The rapid cure for the army was carried out in the *Feldbadegarnituren* of the Red Cross wherever necessary. These had the same equipment as the permanent institutions and were operated by trained attendants and nurses.

Another institution was established in a suburb of Vienna, Meidling, under the direction of an assistant, Dr. O. Neugebauer. Here about 8,000 persons with scabies were treated in 1920, 9,736 in 1921 and 4,515 in the first six months of 1922. Similar institutions were established in Wiener Neustadt and Gloggnitz bei Wien.

The Children's Relief of the American Relief Association (Mr. John H. Hynes) asked for ambulances equipped for the quick treatment of scabies because the distribution of food in the villages of Austria was endangered by the epidemic spread of this disease. Dr. Hans Krueger, another assistant, in association with Dr. Alfons Kogard, inspector for the Children's Relief, rid the valley of Triesting, near Vienna, of infestation within a week and the entire district within a short time.[3] Hundreds of children had been infested.

METHOD

Patients with serious eczema or impetigo staphylogenes, old persons, children under 6 years, patients seriously sick and pregnant women after the middle of the term of pregnancy were not given the quick treatment.

The method is carried out as follows:

1. The patient's body is rubbed for fifteen minutes with green soap and wood wool, chiefly by the patient himself. Special attention is given to the favorite sites of scabies. The head and scalp are not treated.

2. The patient is put into a warm bath (30 C.) and is rubbed again with green soap, this time for half an hour, with a brush or wood wool.

3. The patient is taken from the bathtub, dried carefully and smeared with a modification of the old Hardy ointment, which is a modification of the older

2. Oppenheim, M.: Das erste Jahr des Bestandes der Anstalt für Krätzeschnellkuren im Wilhelminen-Spital, Wien. klin. Wchnschr. **33**:102, 1920; Die Schnellbehandlung der Krätze, ibid. **34**:94, 1921; Die Abnahme der Krätzeplage in Wien, ibid. **35**:998, 1922; Behandlung (Schnellkur) bei Skabies, ibid. **39**:1311, 1926.

3. Krueger, H.: Die Krätzeepidemie in Triestingtale, Wien. klin. Wchnschr. **35**:658, 1922.

Helmerich ointment.[4] The areas of the burrows are rubbed especially carefully. The following is the prescription used:

Precipitated sulfur	25 Gm.
Potassium carbonate	10 Gm.
Yellow petrolatum	125 Gm.

(The original Hardy salve contained 10 Gm. of sublimed sulfur, 5 Gm. of potassium carbonate and 60 Gm. of lard.) The hands are covered by gloves and the feet by socks, and the patient is rolled in a sheet and covered with a woolen blanket. (The gloves and socks may be dispensed with if the salve is applied especially thoroughly to the areas of the burrows.)

4. After two hours the patient is put under a shower, where the ointment is removed by soaping with a common soap. He is dried carefully and his entire body except the head and neck smeared with zinc paste (30 Gm. each of zinc oxide and purified talc and 60 Gm. of yellow petrolatum).

The entire treatment takes three hours. Moderate itching remains for a few days. During the treatment, shirts, underwear, socks, gloves and shoes are sterilized by hot air. Hebra stated that only those parts of the clothing which are in immediate contact with the skin need to be disinfested.

It is possible to treat small children with this method if the time of application of green soap is shortened to five or ten minutes and that of the sulfur-potassium ointment to a quarter or half an hour.

The only so-called recurrences observed after this treatment were actually reinfestations from untreated members of the family. All infested members of a household, therefore, should be treated simultaneously, and this can be done easily in an institution such as those at the Wilhelminenspital and in Meidling. If the treatment is carried out correctly, a poor result is almost impossible.

CONCLUSION

Judging by the successful treatment of 41,354 persons at the Wilhelminenspital from 1918 to 1922 and of more than 22,000 persons in Meidling from January 1920 to July 1922, in which year the epidemic of scabies was brought under control, one may say that this treatment is sure, fast, agreeable and cheap, the best treatment during wartime, when scabies is epidemic.

914 West Ainslie Street.

25 East Washington Boulevard.

4. Helmerich's original salve contained 2 parts of sublimed sulfur, 1 part of potassium carbonate and 8 parts of fat.

EVALUATION OF MEASURES FOR PREVENTION OF IVY DERMATITIS

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There are many remedies which are considered of value in the prevention of poison ivy and poison sumac dermatitis. Some of the more recently recommended prophylactic ointments have been too hastily accepted as efficacious and have been prematurely heralded as the solution of the problem of preventing ivy dermatitis. These reports have given physicians and ivy-sensitive laymen alike a false sense of security. The most recently advocated protective preparations are the ferric chloride ointment recommended by Keeney [1] and the sodium perborate ointment prescribed by Schwartz, Warren and Goldman.[2] If these preparations are applied to the skin prior to contact with members of the poisonous rhus group, a subsequent dermatitis is said to be prevented.

Keeney reported that "from the results of these experimental studies ten per cent ointment of ferric chloride should protect clinically against poison ivy dermatitis if applied before contact with poison ivy occurs."

Schwartz and collaborators accepted McNair's [3] erroneous observation that the milky juice of poison ivy is readily oxidized by the air, after which it loses its toxic properties. They summarized that "further experimental evidence and the results of field trials are presented to support the contention that a suitable ointment base containing sodium perborate is an effective preventive against poison ivy dermatitis when certain rules for its use are observed." The oxygen which is liberated from the perborate was stated to detoxify ivy oleoresin.

Shelmire's [4] experiments with sodium perborate failed to substantiate the favorable results reported by Schwartz.

Many physicians and laymen alike for years have empirically advocated the use of a strong alkali soap as a means of preventing or mitigating the dermatitis following exposure to poison ivy. Solutions of potassium permanganate and of ferric chloride are other agents which with an equal lack of experimental evidence have been considered reliable means of neutralizing the dermatitis-producing fraction of the rhus oleoresin.

The present status of prophylactic measures against ivy dermatitis is decidedly confusing to persons desiring accurate information. This highly important question on the subject of prevention of ivy dermatitis must be asked: Is there today any measure which is of unquestionable value for protecting a sensitive subject from rhus dermatitis or for abating the reaction after exposure has occurred?

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1. Keeney, E. L.: Studies on Human Hypersensitivity to Poison Ivy, J. South. M. A. **35**:408-410 (April) 1942.

2. Schwartz, L.; Warren, L. H., and Goldman, F. H.: Protective Ointment for the Prevention of Poison Ivy Dermatitis, Pub. Health Rep. **55**:1327 (July 26) 1940.

3. McNair, J. B.: Rhus Dermatitis: Its Pathology and Chemotherapy, Chicago, University of Chicago Press, 1923.

4. Shelmire, B.: Sodium Perborate Ointment and Poison Ivy Dermatitis, J. A. M. A. **116**:681-683 (Feb. 22) 1941.

The fact that absolutely no protective benefit is derived from the two to four injections of commercial ivy preparations for hyposensitization to this plant has been conclusively proved though not generally accepted.[5]

The purpose of this report is to evaluate the effectiveness of a few of the recently endorsed prophylactic ointments and some of the older empiric protective remedies recommended for preventing dermatitis caused by contact with certain poisonous species of the rhus group, poison ivy and poison sumac.

FIELD TRIPS

Field trips are the usual means used to substantiate claims of benefit from specific measures. Excursions into ivy-infested terrain do not prove the value of any protective measures unless it has been proved that one has actually come into contact with poison ivy sap on such an excursion. Most persons will instinctively avoid contact with the plants if they recognize them. Contact between the skin of a sensitive persons and the oleoresin from the bruised plant is essential before a dermatitis results. The fact is well established that merely touching an unbroken leaf, branch or stem of an ivy plant does not constitute exposure, since the sap, which contains the dermatitis-producing fraction, is not on the unbroken portion of the plant. Bruising the plant is essential for liberation of the oleoresin. There is therefore injected a doubt whether volunteers on a field trip have actually experienced contact with ivy oleoresins. It is apparent that accurate information or conclusions are impossible when field trips are considered as a means of exposure, since one can never be certain that the bruised plant was touched unless a dermatitis actually ensues.

I, who am clinically sensitive to poison ivy, was surprised to discover after several field trips into poison ivy–infested areas to study plants, to observe collection of specimens and on one occasion to assist in the grubbing of roots for transplanting that only on the last-mentioned mission did a dermatitis from poison ivy follow. No precautions were taken on the numerous exposures, and it was thought that a dermatitis would follow each field trip. Waist-high poison ivy was waded through and touched and protective measures were not employed, but on only one occasion did dermatitis follow.

FINGER TESTS WITH POISON IVY

One of the difficult problems in experimentation with rhus is the question of the level or degree of sensitivity of the subject and the amount of sap encountered during the average clinical exposure. Some persons give positive reactions to concentrated dilutions of poison ivy extract (1 : 1,000 dilution of ivy oleoresin in acetone or 1 : 100 dilution in oil) yet do not have a dermatitis following ordinary clinical exposure to the plant. These persons are said to have a subclinical sensitivity to poisonous members of the rhus group.[6]

If a quantitative dilution of ivy extract could be shown experimentally to approximate the equivalent amount of ivy sap contacted during an average clinical exposure, it would be of great value. Then by quantitative patch tests with a standardized ivy oleoresin one could determine whether a patient with a questionable ivy dermatitis is clinically sensitive to the ivy plant. It would also be of equal assistance in experimental studies on rhus dermatitis prophylactics.

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5. Shelmire, B.: Cutaneous and Systemic Reactions Observed During Oral Poison Ivy Therapy, J. Allergy **12**:252-268 (March) 1941.

6. Shelmire, B.: Contact Dermatitis from Weeds: Patch Testing with Their Oleoresins, J. A. M. A. **113**:1085-1090 (Sept. 16) 1939.

One reason for the inability to find the solution to such a problem by patch tests is the wide variation in the strength of ivy extracts made from a single batch of ivy leaves. The strength of the testing extract depends on the solvent used in the extraction,[7] the maturity of the collected specimens, the period of drying between collection and extraction of the leaves and the vehicle in which the testing oleoresin is suspended. Shelmire has shown that the allergenic potencies of ivy oleoresins vary as much as 1,000 per cent, and an acetone dilution of rhus oleoresin may be one hundred times as potent on quantitative tests as the same concentration in some oil vehicle. In the former, the acetone evaporates when placed on the skin, leaving a film of the pure oil, whereas the ivy oleoresin in the latter remains in pure dilution.

With such a wide variation in the potency of ivy extract and in the absence of chemical isolation or standardization of the dermatitis-producing fraction of the plant, a method for approximating clinical exposure to the ivy shrub or vine was devised. Fresh green leaves of the poison ivy plant were gathered by a person not sensitive to the plant, and a portion of a leaf was gently bruised by rolling it between the thumb and the index finger, and then between the thumb and the middle finger, etc., depositing as nearly as possible an equal amount of the oleoresin on each finger. The bulbs of all fingers were then rubbed together to equalize the oleoresin further. Experimental exposure to poison ivy was then accomplished by a single light stroke on the volunteer's skin with a contaminated finger. No visible stain or moisture could be seen on the fingers or the stroked area. This method of experimental exposure to poison ivy is termed the "finger test" in this report. Results of a similar procedure carried out on subclinically sensitive and nonsensitive subjects showed that the test did not constitute a primary irritant. In a clinically sensitive person the ensuing dermatitis approximates closely the usual reaction following exposure, i. e. a band of dermatitis varying from erythema to vesiculation, depending on the sensitivity of the patient. Since most clinically acquired poison ivy dermatitis is occasioned by contact of a patient's skin with his ivy-contaminated hands (ivy dermatitis in streaks or linear arrangement, dermatitis of the genitals, etc.) the finger test seems to approximate closely natural accidental contact with the ivy plant. Dr. Bedford Shelmire, being nonsensitive to the ivy plant, collected the fresh ivy leaves and performed the "finger tests."

EXPERIMENTAL STUDY

Tests were carried out over a period of approximately one year on 9 subjects who were clinically sensitive to poison ivy. About 300 different contact tests were performed on these volunteers. The level of cutaneous sensitivity to poison ivy of all the subjects remained approximately constant, as demonstrated by repeated quantitative patch tests.

Soap and Water.—Experimental exposure to poison ivy was made by the "finger tests." Two areas 6 inches (15 cm.) apart were prepared on the volar surface of each forearm of the subjects by making horizontal strokes with a contaminated finger. The tested subjects were made to wash the contaminated areas vigorously with laundry soap and running water for five minutes as if preparing for a surgical operation, and in so doing attempt to remove all of the oleoresin from their skin. The other stroked area was not washed, in order that it could be used as a control. All three recognized species of poison ivy (Toxicodendron radicans, Toxicodendron diversilobum and Toxicodendron quercifolium) and poison sumac (Toxicodendron vernix) were employed in the study at different times. The tests with soap and water were repeated on many occasions and the results collectively summarized. All readings of cutaneous reactions were made on the fourth day.

7. Howell, J. B.: Solubility of the Dermatitis Producing Fraction of Poison Ivy, Arch. Dermat. & Syph. **44**:665-666 (Oct.) 1941.

In the mildly sensitive subjects when the contact time after the finger test (time elapsed between the stroking of the arm with the contaminated finger and the start of the washing operation) was one minute thorough and prolonged washing with soap and water offered complete protection in most instances. In the moderately sensitive persons the reaction was reduced. In the highly sensitive subjects there was no difference between the washed areas and unwashed control sites. When the areas were washed five minutes after stroking the skin with the contaminated finger, the subsequent dermatitis at the washed sites was somewhat less than in the unwashed control areas in 4 subjects. In the remaining 5 volunteers there was no difference between the washed sites and the control areas.

When the contact time was ten, fifteen, thirty, sixty and one hundred and twenty minutes, the dermatitis which followed at the sites which were thoroughly washed was equal to that of the unwashed areas in all trials. Soap and water will not prevent or mitigate ivy dermatitis in an extremely sensitive person, even if used after the brief interval of one minute. This remedy will lessen the severity of the ensuing dermatitis in persons of average sensitivity only if employed before the first five or ten minutes following exposure, that is, before the quickly drying ivy oleoresin has completely dried.

A practical example of the difficulty encountered in removing the dermatitis-producing fraction of ivy from the skin can be cited. Dr. Bedford Shelmire, who is not clinically sensitive to ivy, gathered several plants early one morning. His hands were washed thoroughly with soap and water before he started his routine office work. During the following four days I observed 9 patients with an ivy dermatitis confined to areas touched by his contaminated fingers the morning of collection of the plants. I talked with one of his volunteers who was exposed to the bruised ivy plant on the field trip. Although thorough washing of the exposed areas was carried out within ten minutes, a vesicular ivy dermatitis developed at the sites of contact two days later.

From this it appears that soap and water is of little practical value in preventing ivy dermatitis, as few people can wash previous to five minutes after exposure.

Ferric Chloride.—Experimental exposure to ivy by means of the "finger tests" was made on the backs of the volunteers. This was accomplished by horizontally stroking six areas of the back, at distances of 4 inches (10 cm.) apart, with a different contaminated finger. A 10 per cent solution of ferric chloride was liberally applied to the sites of contact at intervals of five, ten, fifteen, twenty and thirty minutes. In no instance was the resulting dermatitis at the treated areas any less than at the control sites. Although these tests were repeated on numerous occasions, the end results were the same. On several occasions the dermatitis at the five and ten minute sites was slightly delayed but not appreciably reduced in severity.

A 10 per cent solution of ferric chloride did not neutralize the dermatitis-producing fraction of ivy after the integument had been contaminated by the oleoresin. When incorporated in an ointment base and liberally applied to the skin previous to contact with poison ivy, as suggested by Keeney, any protection such a preparation affords is due to the mechanical covering offered by the base rather than to chemical neutralization by ferric chloride.

Ten per cent calamine, 10 per cent zinc oxide or 10 per cent talcum prepared in the same ointment base and applied to the skin previous to the finger test, offered a reduced cutaneous reaction equal to that afforded by 10 per cent ferric chloride ointment. The greatest objection to the latter ointment, besides its impotency in preventing ivy dermatitis, was the permanent staining imparted to clothing.

A 10 per cent solution of ferric chloride did not prevent dermatitis when applied five minutes or longer after the finger test. A 10 per cent ferric chloride ointment

applied previous to contact offered no more protection than an inert substance in the same ointment base.

Potassium Permanganate.—The backs of the volunteers were prepared in the same manner as described for the trials of ferric chloride. An aqueous solution of freshly prepared 10 per cent potassium permanganate was copiously applied at various intervals of time to the sites touched with the ivy-contaminated fingers.

When this solution was applied after a contact time of five minutes, the dermatitis was prevented in most instances and greatly lessened in others. The results were approximately the same if the permanganate solution was applied after an exposure time of ten minutes.

In the highly sensitive subjects, when the same solution was used after a contact time of fifteen minutes the dermatitis was no less severe than that of the control dermatitis on repeated occasions. A definite decrease in the severity of the reaction was observed in the less sensitive subjects, although the eruption was not entirely prevented in a single instance when the neutralizing solution was applied at this time interval after the exposure. Even as late as thirty minutes after exposure some modification of the severity of the reaction was noted in the 3 mildly sensitive volunteers. The others showed reactions in the treated areas identical with those of the control sites.

After contact time of forty-five minutes and of one, two, three and four hours, the severity of the dermatitis at the sites treated with potassium permanganate was the same as that of the control areas in all of the volunteers.

A 10 per cent solution of potassium permanganate is capable of diminishing the severity of ivy dermatitis after exposure in a mildly sensitive person who has not sustained an overwhelming exposure if applied within fifteen minutes after contact is made. For a highly sensitive subject it must be used within the first five or ten minutes to obtain the same results. In a few persons lessening of the eruption was accomplished when this solution was used as late as thirty minutes. The solution was of no value after forty-five minutes.

Sodium Perborate Ointment.—The left side of the back of each subject was smeared with freshly prepared 10 per cent sodium perborate ointment in ointment bases 1 and 2, as advocated by Schwartz, Warren and Goldman. The right side of the back was similarly smeared with the same formula in which 10 per cent of an inert powder (zinc oxide, talcum or prepared calamine) was substituted for the sodium perborate. Fingers contaminated with ivy were then streaked horizontally across the treated areas at six different sites on each side of the back. Approximately one hundred different tests were made with these ointments at different intervals. Control tests were made simultaneously on both sides of the back below areas smeared with the various ointments.

Sodium perborate ointment did not prevent the ivy dermatitis in a single instance on any subject tested. The dermatitis produced at the sites covered with the perborate ointment was no less severe than that at sites covered with the various inert substances in the same ointment bases.

Sodium perborate prophylactic ointment lessened the resulting reaction only very slightly as compared with the dermatitis in the unprotected control areas. Two highly sensitive subjects experienced widespread dermatitis over the entire back and the lower part of the abdomen after these tests. The oils incorporated in these protective ointments was found to disseminate the ensuing dermatitis because of the solubility of the dermatitis-producing fraction of the ivy oleoresin in oily mediums.

The result of this experimental study confirms the observations of Shelmire that "ten per cent sodium perborate ointment offers little protection against ivy derma-

titis. The amount of protection afforded seems directly proportionate to the thickness of the powdery film left after evaporation of the water of the vanishing cream."

White Petrolatum.—The resulting dermatitis following the "finger test" did not remain localized to the contaminated site on areas where petrolatum alone was used as a prophylactic ointment previous to contact. Widespread involvement of the regions surrounding the treated areas occurred. Petrolatum alone caused wide spreading of the dermatitis and produced no apparent lessening of the severity of the eruption. This, again, is due to solubility of the ivy oleoresin in oily mediums.

CONCLUSIONS

There is no suitable topical prophylactic substance for preventing poison ivy dermatitis or for mitigating the eruption after contact has occurred. From experimental studies, a 10 per cent solution of potassium permanganate prevented or diminished the severity of ivy dermatitis in most instances if employed during the first fifteen minutes after exposure.

Thorough washing with soap and water and preexposure anointing of the skin with white petrolatum, 10 per cent ferric chloride ointment or 10 per cent sodium perborate ointment or the use of 10 per cent solution of ferric chloride after exposure to the plant did not prevent ivy dermatitis.

1719 Pacific Avenue.

THE CHICK EMBRYO ANTIGEN (LYGRANUM) TEST FOR LYMPHOGRANULOMA VENEREUM

A CLINICAL INVESTIGATION

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The purpose of this communication is to report on our experience with a relatively new antigen introduced in 1940 by Grace, Rake and Shaffer [1] as being superior to mouse brain antigen for the performance of the Frei test. This antigen (known as lygranum) is made by growing the lymphogranuloma venereum virus in the yolk sac of the developing chick embryo, while lygranum control is made from the yolk sac itself.

In 1941 Sulkin and co-workers,[2] using as did the originators of the test a 7 mm. papule as a minimal positive reaction, found in 42 patients with lymphogranuloma venereum 40 with a positive reaction to lygranum and 38 with a positive reaction to human bubo pus. There were easily recognized nonspecific papules in some of the control subjects. The Robinsons [3] in 1942 performed simultaneous tests with lygranum and bubo pus on 127 patients. They found 91 per cent agreement between the results of the two antigens. Beerman [4] in a discussion of this paper cited Axelrod as finding complete agreement between the results obtained with lygranum antigen and those obtained with bubo pus antigen in 40 of 46 tests. Brandt [5] in discussing the same paper expressed the belief that a negative history and an absence of scars of lymphogranuloma venereum did not invalidate the specificity of a positive Frei reaction. Combes, Cañizares and Morris [6] reported on 700 Frei tests made with lygranum and mouse brain antigens; 102 were made

From the Department of Dermatology and Syphilology, Western Reserve Medical School and Cleveland City and University Hospitals. This work was done under a grant from The Therapeutic Research Committee, Council on Pharmacy and Chemistry, American Medical Association.

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2. Sulkin, S. E.; Fletcher, P. F.; Huber, E. T., and Reh, E. P.: The Frei Test for Lymphogranuloma Venereum: Experiences with a New Antigen (Lygranum) Prepared from Infected Yolk Sac of Developing Chick Embryo, J. A. M. A. **116**:2663 (June 14) 1941.

3. Robinson, H. M., and Robinson, H. M., Jr.: Comparison of Frei Antigens, Arch. Dermat. & Syph **45**:112 (Jan.) 1942.

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5. Brandt, R., in discussion on Robinson and Robinson.[3]

6. Combes, F. C.; Cañizares, O., and Morris, G.: Frei Test: Evaluation of Chick Embryo Antigen (Lygranum), Arch. Dermat. & Syph. **46**:264 (Aug.) 1942.

with bubo pus antigen. Six and one-tenth per cent of the reactions to lygranum were doubtful; that is, the papules were between 5 and 7 mm. in diameter. There were 2 per cent false negative reactions. The authors concluded that lygranum gave results which were more reliable, were easier to evaluate and had less tendency to give false reactions than mouse brain antigen, but they recommended the use of all three antigens concurrently. Mortara and Greenblatt [7] examined 82 patients with lygranum, bubo pus and mouse brain antigens. They found no false positive or false negative reactions with the chick antigen. They measured all reactions exactly and showed that the response to the lygranum control was slight. In 18 per cent of the reactions to lygranum control there were papules from 2 to 4 mm. in diameter. In 1943 Curth,[8] who used a 5 mm. nodule as the basis for a positive reaction to lygranum instead of the 7 mm. papule employed by all the previous investigators, found positive reactions in 67 of 69 patients with lymphogranuloma venereum. The 2 patients who had negative reactions to lygranum and positive reactions to bubo pus gave positive reactions when they were retested with lygranum one to two weeks later. Eleven of them showed a positive reaction to lygranum control. Of 90 patients who had negative reactions to bubo pus and no history or clinical evidence of lymphogranuloma venereum, 22 reacted positively to lygranum but none reacted to lygranum control. Curth stated that in some of the 22 subjects there was a possibility of a latent infection undetected by human antigen. She stated the belief, therefore, that lygranum gave a large number, possibly 24 per cent, of false positive reactions in the control group. It must be remembered, however, that her criterion of a positive reaction was a 5 mm. papule. Considering the false negative reactions there was definite agreement in 78 per cent of her series of subjects.

METHOD

In the past one and one-half years at City Hospital and University Hospitals, of Cleveland, we have performed tests with lygranum and lygranum control on 379 patients from the dermatologic, medical and surgical services. On 209 of these, concurrent tests were made with human bubo pus antigen prepared separately by each hospital. The tests were performed by injecting 0.1 cc. of the antigen intradermally into the flexor surface of the forearm. The reactions were examined after forty-eight and seventy-two hours, but since there was only a slight variation between the two readings the former was used as the basis of the study. At the beginning of the study a 5 mm. papule with or without erythema was considered a positive reaction.

Results of Intradermal Tests with Lygranum

I. Patients with clinical lymphogranuloma venereum			39
A. Cutaneous tests with lygranum			
1. Positive reactions		36	
5 mm.	0		
6 mm.	1		
7 mm.	4		
Over 7 mm.	31		
2. Negative to bubo pus	0		
B. Clinical types			
1. Inguinal	25		
2. Rectal	11		
3. Rectal and elephantiasic	2		
4. Elephantiasic	1		

7. Mortara, F., and Greenblatt, R. B.: Comparative Study of Antigens of Human Pus, Mouse Brain and Chick Embryo Origin for the Diagnosis of Lymphogranuloma Venereum, Ven. Dis. Inform. **24**:14, 1943.

8. Curth, H. O.: Evaluation of Yolk Sac Antigen for Frei Test, Am. J. Syph., Gonor. & Ven. Dis. **27**:47, 1943.

II. Patients without clinical lymphogranuloma venereum				340
A. Cutaneous tests with lygranum				
1. Positive reactions			32	
5 mm.		1		
6 mm.		3		
7 mm.		7		
Over 7 mm.		21		
a. Patients with another venereal disease	24			
b. Patients for whom determinations of blood albumin and globulin were made	11			
(1) Patients with hyperglobulinemia 5				
c. Patients with history of nonsyphilitic bubo	7			
2. Negative tests			308	
a. Patients with another venereal disease	169			
b. Patients for whom determinations of blood albumin and globulin were made	15			
(1) Patients with hyperglobulinemia 15				

Comparison of Results with Human Bubo Pus Antigen and with Lygranum Antigen

I. Patients with clinical lymphogranuloma venereum				18
A. Positive reactions to lygranum			7	
1. Positive to bubo pus		13		
2. Negative to bubo pus		3		
B. Negative reactions to lygranum			2	
1. Positive to bubo pus		2		
2. Negative to bubo pus		0		
II. Patients with a history of lymphogranuloma venereum				7
A. Positive reactions to lygranum			7	
1. Positive to bubo pus		6		
2. Negative to bubo pus		1		
B. Negative reactions to lygranum			0	
III. Patients without lymphogranuloma venereum				184
A. Positive reactions to lygranum			24	
1. Positive to bubo pus		15		
2. Negative to bubo pus		9		
B. Negative reactions to lygranum			160	
1. Positive to bubo pus		0		
2. Negative to bubo pus		160		

Eighty-two per cent of the patients tested had absolutely no reaction to lygranum control.

RESULTS

As can be seen from the tabulation, there was only one positive reaction between 5 and 7 mm. in diameter in patients with clinical lymphogranuloma venereum. However, of patients without lymphogranuloma venereum there were 4 with reactions within this range. All of these patients were presumably sexually promiscuous.

Three patients with clinical lymphogranuloma venerum, 2 of whom had hyperglobulinemia, had completely negative reactions. One of them was tested one month later and at that time reacted with a 4 mm. papule. When retested, another showed no reaction one month later and the third no reaction one week later. The inguinal type of the disease was predominant.

In 24 (80 per cent) of the patients without clinical lymphogranuloma venereum who had positive reactions, there was presumptive evidence of sexual promiscuity. For 11 the albumin and globulin contents of the blood were determined, and 5 of (45 per cent) of these had hyperglobulinemia. Seven of the 32 patients with positive reactions to lygranum and without clinical lymphogranuloma venereum had a history of a bubo which we believe was not due to syphilis. Of the patients without clinical lymphogranuloma venereum who had a negative reaction to lygranum, only 169 (55 per cent) had another venereal disease and could be presumed to be sexually promiscuous. There were 193 patients without clinical lymphogranuloma venereum who had another venereal disease, and 24 (12 per cent) of these had a positive reaction to lygranum. There were 147 patients without clinical lymphogranuloma venereum who had no history of a bubo or another venereal disease, and of these only 8 (5 per cent) had a positive lygranum. In all 15 patients without lymphogranuloma venereum whose reactions to lygranum were negative and for whom determinations of blood albumin and globulin were made, hyperglobulinemia was found. This group included patients with cirrhosis, colitis, pulmonary tuberculosis, gastrocolic-renal fistula, rheumatic heart disease, hypertensive cardiovascular disease, nephritis, carcinoma of the kidney, mediastinal tumor and coronary sclerosis. These patients were especially selected in order to determine whether hyperglobulinemia in itself affects the test.

Comparison of reactions to lygranum with those to bubo pus in 209 patients showed complete agreement in 93.8 per cent. In 2 patients with clinical lymphogranuloma venereum both tests elicited completely negative reactions.

COMMENT

All observers to date except Curth have regarded a 7 mm. papule as the minimal positive reaction. Our results suggest that a papule of this size should be used, since in the positive reactions there were only 5 (8 per cent) tests in which the papules measured 5 or 6 mm. Three patients could be considered as having false negative reactions. In 1 of these, a retest showed a tendency toward positivity. All 3 of these patients were treated with sulfathiazole orally, which could possibly explain the persistent anergy.

Twelve per cent of the patients with a venereal disease (presumably sexually promiscuous) but without clinical lymphogranuloma venereum had a positive reaction to lygranum, while only 5 per cent of the nonvenereal group had a positive reaction to this antigen. This suggests that a fair number of the presumably sexually promiscuous group may have had subclinical lymphogranuloma venereum and that there is some correlation between sexual promiscuity and the occurrence of subclinical lymphogranuloma venereum.

In the group of 32 patients without clinical lymphogranuloma venereum who had a positive reaction to lygranum, 7 with primary or mucocutaneous syphilis had a history of a bubo. These and possibly others probably had a remote lymphogranuloma venereum infection. The lygranum test elicited a negative reaction in 15 patients with hyperglobulinemia not due to lymphogranuloma venereum.

SUMMARY

Three of the 379 patients tested had lymphogranuloma venereum clinically and yet had negative reactions to lygranum. This represents an incidence of false negative reactions of 0.8 per cent. For 32 patients (8 per cent of all patients tested) who had positive reactions to lygranum the diagnosis of lymphogranuloma venereum could not be unequivocally made. However, the high rate of sexual promiscuity

in this group and the definite history of bubos in 7 of the patients suggest that a fair number of these false positive reactions may have been due to subclinical lymphogranuloma venereum, but it would be impossible to say how many if any of the 32 reactions were falsely positive. There was 93.8 per cent agreement between results obtained from lygranum and those from bubo pus antigens in 209 patients tested.

CONCLUSIONS

There probably is a fair incidence of subclinical lymphogranuloma venereum.

A papule 7 mm. in diameter should be considered the minimum size of a positive reaction to chick embryo antigen (lygranum).

Chick embryo antigen (lygranum) provides a fairly reliable test for lymphogranuloma venereum, but positive reactions do not always indicate the presence of the disease and should be interpreted with careful consideration of the entire clinical picture presented.

In view of the scarcity of reliable human bubo antigen, it is our opinion that chick embryo antigen is without doubt the most reliable substitute at hand for intradermal diagnosis of lymphogranuloma venereum. It is unfortunate, however, that the difference between a positive and a negative result must be measured in terms of tenths of a centimeter.

STUDIES ON OINTMENTS

IV. LOCAL ACTION OF SALICYLIC ACID PLUS SULFUR FROM VARIOUS OINTMENT BASES

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The local action of salicylic acid in various bases as well as the action of sulfur in the same bases in different concentrations has previously been studied.[1]

Since the combination of these two drugs is so widely used in dermatologic practice, an attempt was made to study their combined local action from various ointment bases on the normal human skin. After its application for several days, salicylic acid causes keratolysis, swelling and exfoliation of the stratum corneum. The acid causes an edematous formation in the rete Malpighii, but without its total destruction, and a new stratum corneum is quickly formed under its irritating and stimulating effect.

The action of sulfur is more complex. Its action is twofold, keratolytic and keratoplastic. A detailed account of the pharmacologic action of sulfur was previously [2] omitted because of lack of space. For this reason and because no adequate review was found in the English literature, such a review will be presented here.

Sulfur occurs in the body in cysteine:

$CH_2 - SH$
$CHNH_2$
$COOH$

Thioaminopropionic acid

which is the most important carrier for the sulfur. By means of its condensation and oxidation, cystine is formed:

$CH_2 - S - S - CH_2$
$CHNH_2 \qquad CHNH_2$
$COOH \qquad COOH$

di-(thioaminopropionic acid)

It has been known for a long time that cysteine may be readily oxidized to cystine. In fact, this conversion occurs spontaneously in slightly alkaline solutions of cysteine exposed to the air. The reverse process, the reduction of cystine, occurs

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The fourth condensed part of a thesis submitted to the faculty of the Graduate School of the University of Minnesota in partial fulfilment of the requirements for the Degree of Doctor of Philosophy in Dermatology and Syphilology.

1. Strakosch, E. A.: Studies on Ointments: II. Ointments Containing Salicylic Acid, Arch. Dermat. & Syph. **47**:16 (Jan.) 1943.

2. Strakosch, E. A.: Studies in Ointments: III. Ointments Containing Sulfur, Arch. Dermat. & Syph. **47**:216 (Feb.) 1943.

almost as readily in the presence of even mild reducing agent. Accordingly, a system composed of cysteine and cystine may be regarded as an auto-oxidizable system, the cysteine being oxidizable by molecular oxygen and the cystine reducible by hydrogen. The reduction involved would be essentially represented by the following equation:

$$O + \begin{matrix} COOHCHNH_2CH_2SH \\ COOHCHNH_2CH_2SH \end{matrix} \underset{\text{reduction}}{\overset{\text{oxidation}}{\rightleftharpoons}} \begin{matrix} COOHCHNH_2S \\ COOHCHNH_2S \end{matrix} + H_2O$$

cysteine cystine

The carrier of the "sulfhydryl, or thiol, group," — SH, in the tissue besides cysteine is glutathione of Hopkins,[3] which is a tripeptide, containing cystine, glutamic acid and aminoacetic acid. Glutathione can be reduced and oxidized and promotes oxidation of certain proteins in a peculiar way. The oxidation proceeds only when and while protein itself contains SH groups.

The aforementioned process plays an all-important part in the process of keratinization of the epidermis, as keratin contains a large amount of cystine.

Two chemical characteristics of sulfur are of great importance for its behavior in the organism: first, its occurrence in different phases of oxidation and, secondly, its ability to take up several sulfur atoms.

In the air, and especially in the presence of light, the elementary sulfur is oxidized first to sulfurous acid and later to sulfuric acid. The lowest phase of oxidation is hydrogen sulfide (H_2S), the next higher elementary sulfur and the highest the sulfate.

Hydrogen sulfide, in turn, can take up further sulfur atoms and forms hydrogen persulfides (H_2S_2, H_2S_3, H_2S_4, H_2S_5). Werder [4] showed that the formation of polysulfides from sulfur and hydrogen sulfide occurs in the body. The same tendency of taking up sulfur atoms is also found in the organic sulfur compounds; thus cystine is formed from cysteine, a reaction which is reversible. The conversion of cysteine into cystine takes place in the presence of air, although minute amounts of iron, which acts as a catalyst, must be present according to Warburg and Sakuma.[5]

De Rey-Pailhaide [6] reported in 1888 that if animal tissue is brought in contact with sulfur hydrogen sulfide is formed. This observation was later closely studied by Heffter [7a] and by Heffter and Hausmann,[7b] who found it to be the cysteine which forms ample hydrogen sulfide if brought in contact with sulfur. The glutathione acts in a like manner and so does probably methionine.

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3. Hopkins, F. G.: (*a*) On an Autoxidizable Constituent of the Cell, Biochem. J. **15**:286, 1921; (*b*) Glutathione, ibid. **19**:787, 1925.

4. Werder, H.: Zur Kenntnis der Schwefelwirkung, Arch. f. exper. Path. u. Pharmakol. **95**:238, 1922.

5. Warburg, O., and Sakuma, S.: Ueber die sogenannte Autoxydation des Cysteins, Arch. f. d. ges. Physiol. **200**:203, 1923.

6. De Rey-Pailhaide, J., cited by Heffter, A., and Heubner, W.: Handbuch der experimentellen Pharmakologie, Berlin, Julius Springer, 1927, vol. 3, pt. 1.

7. (*a*) Heffter, A.: Beiträge zur Pharmakologie des Schwefels, Arch. f. exper. Path. u. Pharmakol. **51**:175, 1904. (*b*) Heffter, A., and Hausmann, M.: Ueber die Wirkung des Schwefels auf Eiweisskörper, Beitr. z. chem. Physiol. u. Path. **5**:213, 1904.

The biochemistry of sulfur and its pharmacodynamics are extremely complicated. Heubner,[8] Heffter,[7] Hopkins,[3] Sabbatini [9] and Wieland [10] made investigations which demonstrated clearly that the action of sulfur depends on its conversion to hydrogen sulfide, which has a keratolytic effect. Hydrogen sulfide is formed if sulfur comes in contact with living tissue. This process takes place only in those proteins which contain the sulfhydryl radical (R — SH) in its molecule and can give up hydrogen, or, in other words, proteins which do not contain the sulfhydryl radical cannot form hydrogen sulfide. The reaction involved would be essentially represented by the following equation:

$$\underset{\text{sulfhydryl}}{2\,R-SH} + S \rightarrow \underset{\text{disulfide}}{R-S.S-R} + H_2S$$

According to Wieland [10] sulfur is the substance which makes oxidation possible by means of dehydrogenation. It is a hydrogen acceptor, but it can also be an oxygen acceptor and thus a reducing agent. Gordonoff [11] gives the following equation:

$$S + H_2 = H_2S \qquad \text{(sulfur as hydrogen acceptor)}$$
$$H_2S + 2\,O_2 = H_2SO_4 \quad \text{(sulfur as oxygen acceptor)}$$

Sulfur therefore can oxidize after its transformation into hydrogen sulfide. Hydrogen sulfide, in turn, has the ability to dissolve elementary sulfur by forming polysulfides. Sulfur is therefore what Markwalder [12] termed a "complex former." This seems to be the explanation why the entirely insoluble sulfur can bring about a biologic action.

Sulfur, in accordance with the old maxim "corpora nisi soluta agunt," can display its action on the skin only if it is transformed into the absorbable form. This is done in two ways: first through the formation of hydrogen sulfide, which is absorbable, and secondly through the formation of hydrogen persulfides (H_2S_2, H_2S_3, etc.), which are formed when sulfur and hydrogen sulfide are both present. These hydrogen persulfides are soluble and diffusible and can, in turn, according to Heubner, deposit sulfur in places with an acid reaction. But this transformation is possible only, as has been pointed out before, when sulfur comes in contact with cells containing the sulfhydryl radical. The sulfhydryl radical is present in cysteine and in glutathione, but cysteine was found by Buffa [13] only in the deeper layer of the epidermis and not in the stratum corneum. Heubner's theory, therefore, was not tenable, at least not for the action of sulfur on intact skin, for no hydrogen sulfide could be formed, as the stratum corneum did not contain cysteine, the substance with the necessary sulfhydryl radical. It did, however, explain the action of sulfur when the stratum corneum was either partly or totally absent or was sufficiently macerated to give sulfur access to the deeper layer of the epidermis, where cysteine was present as demonstrated with the Buffa reaction (The R—SH group gives a blue coloration with sodium nitroprusside, while the disulfide group

8. Heubner, W.: Chemie und Pharmakologie des Schwefels, Zentralbl. f. Haut- u. Geschlechtskr. **20**:385, 1926.

9. Sabbatini, L.: Ueber die Wirkung des kolloidalen Schwefels, je nach dem Weg der Einführung in den Organismus, Biochem. Ztschr. **59**:378, 1914.

10. Wieland, H.: Ueber den Mechanismus der Oxydationsvorgänge, Ergebn. d. Physiol. **20**:477, 1922.

11. Gordonoff, cited by Perutz, A.: Die Pharmakologie der Haut, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1930, vol. 5, pt. 1, p. 158.

12. Markwalder, J.: Balneologie und Pharmakologie, Klin. Wchnschr. **1**:2507, 1922.

13. Buffa, E.: Sur une combinaison sulfurée, J. de physiol. et de path. **6**:645, 1904.

[R — S.S. — R] does not give it). Heubner therefore advocated a second theory to explain the action of sulfur on intact skin. He believed that sulfur could be taken up by cystine (disulfide), which could bring about the change in the mechanical behavior. This theory was disputed by Pulewka,[14] who believed that sulfur in the form of S_2 causes the keratolysis.

Moncorps [15] presented evidence that Heubner's second theory was unnecessary and probably wrong, for he found cysteine, the missing link in Heubner's first theory, in the stratum corneum. This was also found by Golodetz.[16] Moncorps showed also the presence of glutathione in the stratum corneum, a fact unknown to Heubner and Golodetz.

The keratoplastic effect is the second feature of the action of sulfur. Unna [17] assumed a reducing effect of sulfur, which he claimed was responsible for the keratoplastic action. But it is in reality an oxidation process, as was previously pointed out, for Heubner showed the important fact that elementary sulfur behaves primarily as oxygen, acting on the sulfhydryl radical, and transforms cysteine into cystine, the latter forming the most important constituent of the keratin substance. As sulfur is capable of bringing about this transformation, it promotes the formation of keratin and therefore is keratoplastic. So much for the biologic and pharmacodynamic action of sulfur.

To arrive at a better understanding of what happens when salicylic acid or sulfur is incorporated into various bases and applied to the skin and thus to be in a better position to interpret the findings of this study, a short review of the previous work [18] is desirable.

A series of experiments were carried out with salicylic acid in varying concentrations in various bases, to determine first the necessary concentration in the different bases which will produce keratolysis and also the time which was necessary for its production. Identical experiments were made with sulfur. The results are summarized in charts 1, 2 and 3. The details of the technic were previously reported.[1]

EXPERIMENTAL STUDIES

One and five-tenths per cent salicylic acid and 3 per cent sulfur, 3 per cent salicylic acid and 3 per cent sulfur, and 3 per cent salicylic acid and 6 per cent sulfur were incorporated into six ointment bases. These combinations were chosen because they represent the concentrations of salicylic acid and sulfur most widely used in daily practice.

The bases into which each of the three combinations of drugs was incorporated are as follows: (1) petrolatum; (2) petrolatum and hydrous wool fat in equal parts; (3) a base consisting of 6 per cent of a group of esters of cholesterol (chiefly oxycholesterol) in an aliphatic hydrocarbon (petrolatum) base [19]; (4) a base consisting of oleic acid, white petrolatum, oleic acid esters and amines of

14. Pulewka, P.: (*a*) Untersuchungen über Keratolyse, Ztschr. f. physiol. Chem. **146**:130, 1925; (*b*) Weitere Untersuchungen über Keratolyse, Arch. f. exper. Path. u. Pharmakol. **140**:181, 1929.

15. Moncorps, C.: Untersuchungen über die Pharmakologie und Pharmakodynamik der Salben und Salbeninkorporierten Medikamente, Arch. f. exper. Path. u. Pharmakol. **141**: 87, 1929.

16. Golodetz, L.: Die Wirkung des Schwefels auf die Haut, Med. Klin. **7**:1085, 1911.

17. Unna, P. G.: Ueberhäutung und Ueberhornung, Berl. klin. Wchnschr. **35**:583, 1883.

18. Footnotes 1 and 2.

19. The preparation used was aquaphor, manufactured by the Duke Laboratories Inc., Stamford, Conn.

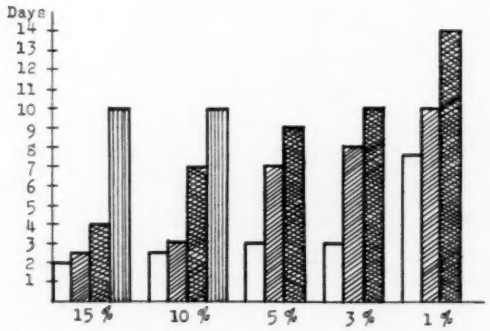

Fig. 1.—Beginning of keratolytic changes from salicylic acid, observed by histologic studies. Each bar indicates the average of four experiments. The blank bars indicate the oxycholesterol-petrolatum ointment base, the base consisting of fatty acid esters of diethanolamine in petrolatum and the base containing stearyl alcohol in liquid petrolatum, water and petrolatum; the bars with diagonal lines, the petrolatum and hydrous wool fat base; the bars with crisscross lines, petrolatum, and the bars with vertical lines, zinc oxide paste. The same bases were used throughout all experiments.

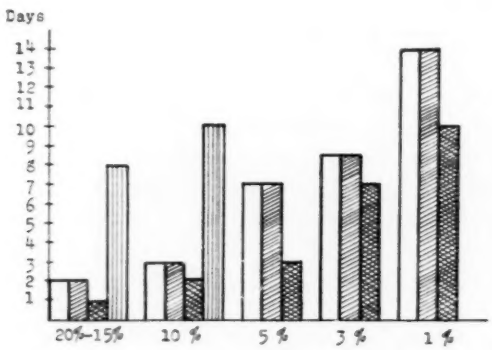

Fig. 2.—Beginning of the keratolytic action of sulfur.

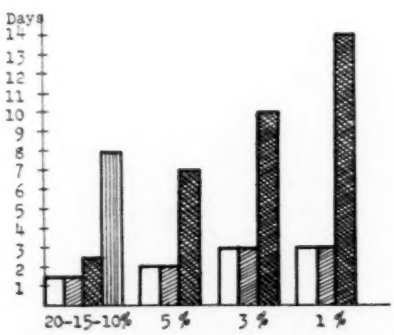

Fig. 3.—Beginning of the keratoplastic action of sulfur.

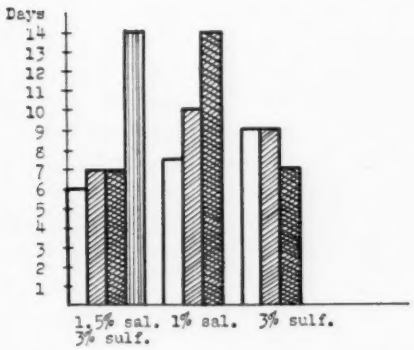

Fig. 4.—Beginning of the keratolytic action of 1.5 per cent salicylic acid plus 3 per cent sulfur compared with the beginning of the keratolytic action of 1 per cent salicylic acid alone and of 3 per cent sulfur alone.

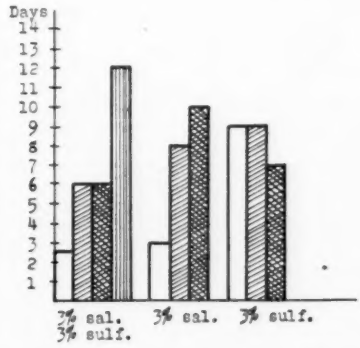

Fig. 5.—Beginning of the keratolytic action of 3 per cent salicylic acid plus 3 per cent sulfur compared with the action of 3 per cent salicylic acid alone and 3 per cent sulfur alone.

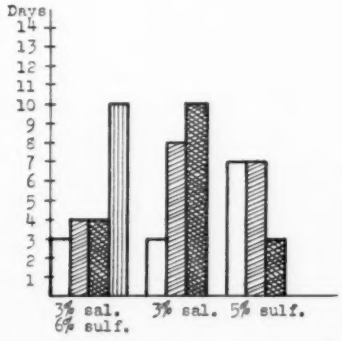

Fig. 6.—Beginning of the keratolytic action of 3 per cent salicylic acid plus 6 per cent sulfur compared with the action of 3 per cent salicylic acid alone and 5 per cent sulfur alone.

diethanolamine,[20] and two bases whose formulas are as follows: (5) stearyl alcohol 10.0 Gm., liquid petrolatum 10.0 Gm., water 10.0 cc. and light petrolatum 70.0 Gm.; (6) zinc oxide 7.5 Gm., talc 7.5 Gm. and enough petrolatum to make 30.0 Gm.

Only normal persons were used for this investigation. The subject was given a bath before the first application but underwent no further preparation, such as clipping the hairs, shaving the skin or washing with alcohol. Five-tenths gram of each ointment was slightly rubbed into areas of 2 by 2 inches (5 by 5 cm.) by means of a glass spatula. The applications were made on the anterior aspects of the upper parts of the thighs. No bandage was applied, and precautions were taken to prevent the wiping off of the ointment. In order to simulate practical conditions, the applications were made three times daily. After block anesthesia with a 1 per cent solution of procaine hydrochloride, specimens for biopsy were taken with a punch after twenty-four, forty-eight and seventy-two hours, and after six, eight and ten days. The tissues were fixed in solution of formaldehyde U. S. P. diluted 1:10, embedded in paraffin, sectioned and stained with hematoxylin and eosin. Each

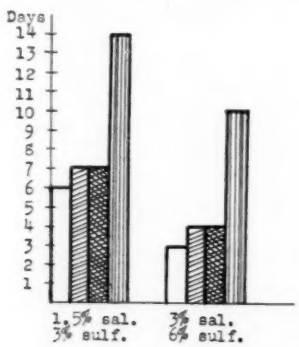

Fig. 7.—Beginning of the keratolytic action of 1.5 per cent salicylic acid plus 3 per cent sulfur compared with the action of 3 per cent salicylic acid plus 6 per cent sulfur.

experimental series was made on the same subject, and each series was repeated four times on different subjects. Every reported result is the average of these four experiments. In order to avoid repetition, I have summarized the results in charts 4, 5, 6 and 7.

COMMENT

The incorporation of two or more drugs in the same ointment base is practiced for only two reasons: first, to obtain the separate but simultaneous effects of each incorporated chemical, and, second, to enhance the action of one drug by means of the other. If one has in mind enhancement of the action of one drug with the other, it is of interest to know just what the ultimate combined result will be. Will it be a summation effect, or will it be less and, if so, how much less? In other words, if it is assumed for the sake of discussion that the effect of a drug A (in a given concentration) is five and that of drug B is also five, will the combined effect be ten or will it be less? It has previously been shown (with salicylic acid or sulfur) that doubling the concentration of a single drug does not necessarily double its action.

20. The preparation used was hydrosorb, manufactured by the Abbott Laboratories, North Chicago, Ill.

In this specific experiment salicylic acid and sulfur were combined. Their common attribute is their keratolytic effect. Sulfur has in addition to this a keratoplastic effect. Hence two separate actions, the combined keratolytic effect of salicylic acid and sulfur and the keratoplastic effect of sulfur, could be studied, and each action then could be compared with the individual effect of the two drugs in the corresponding concentration in the same ointment base. To make the problem even more complicated, it should be recalled that salicylic acid and sulfur individually gave different keratolytic effects when used in identical concentrations in the same base.

The results of each experiment are seen in charts 4, 5, 6 and 7 and are compared with the individual action of the two drugs. Since I had no results with a 1.5 per cent concentration of salicylic acid in the various bases, its action had to be compared with the effects of a 1 per cent concentration. For the same reason, the effects of the 6 per cent concentration of sulfur were compared with the effects of the 5 per cent concentration, which appeared to be permissible for all practical purposes.

It can be noted from the charts that when the two drugs under discussion are incorporated into the same base their combined keratolytic action is generally greater than that of either of the drugs alone (in corresponding concentration and in the same base). Exceptions were observed when 1.5 per cent salicylic acid and 3 per cent sulfur were incorporated into petrolatum. In the first case, an equal keratolytic effect could be produced by the corresponding concentration of sulfur alone. In the latter case, the combined effect appears to be even less. But in all other instances the combined keratolytic effect was better than the arithmetical mean. Doubling the concentration of 1.5 per cent salicylic acid and 3 per cent sulfur reduced almost to half the time which was necessary to produce keratolysis.

When sulfur is combined with salicylic acid, the keratoplastic effect of sulfur is less than that of the identical concentration of sulfur alone. The keratolytic effect of the combination overshadows the keratoplastic action of sulfur.

While the type of ointment base was of some significance when salicylic acid or sulfur was incorporated individually, it appears to be irrelevant, with the exception of zinc oxide paste, when the two drugs were used in combination. This is readily understandable when one considers the different solubilities of these two drugs, the one soluble in water and the other soluble in oil. Better results can be obtained, always considering the same concentration, when a water-soluble drug is incorporated into a base containing water. The same holds true for an oil-soluble drug incorporated into a hydrocarbon base. This apparent advantage, however, is lost when drugs soluble in different mediums are incorporated into one base.

One more observation is of interest. While neither salicylic acid nor sulfur, in the corresponding concentration and time, gave any keratolytic effect when incorporated into zinc paste, such an effect was noted when the two drugs were used in combination.

SUMMARY

The pharmacologic action of sulfur on the skin has been discussed.

One and five-tenths per cent salicylic acid and 3 per cent precipitated sulfur, 3 per cent salicylic acid and 3 per cent precipitated sulfur and 3 per cent salicylic acid and 6 per cent precipitated sulfur were incorporated into the following bases: (1) petrolatum; (2) petrolatum and hydrous wool fat in equal parts; (3) an oxycholesterol-petrolatum ointment base; (4) fatty acid esters of diethanolamine in petrolatum; (5) stearyl alcohol in liquid petrolatum, water and petrolatum, and (6) zinc oxide in talc and petrolatum. Biopsies were performed after

one, two, three, six, eight and ten days, and the keratolytic and keratoplastic action of these ointments on normal human skin was studied histologically.

The combined keratolytic effect of salicylic acid and sulfur and the keratoplastic effect of sulfur in the aforementioned concentrations and bases were studied. Each action was then compared with the individual effect of these two drugs in the corresponding concentration in the same ointment base. It was found that the keratolytic effect of salicylic acid and sulfur combined is generally better than that of either of the two drugs alone.

When sulfur was combined with salicylic acid, the keratoplastic effect of sulfur was less than that of the identical concentration of sulfur alone.

While the type of ointment base was of some significance when salicylic acid or sulfur was incorporated individually, it appeared to be irrelevant, with the exception of zinc oxide paste, when the two drugs were used in combination. While neither salicylic acid nor sulfur, in the corresponding concentration and time, gave any keratolytic effect when incorporated into zinc paste, such an effect was noted when the two drugs were used in combination.

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STUDIES ON OINTMENTS

V. OINTMENTS CONTAINING RESORCINOL

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MINNEAPOLIS

Resorcinol (*Resorcin*) was discovered by Hlasiwetz and Barth (cited by Kellogg [1]) in Vienna in the year 1863 as a decomposition product formed when different resins were melted together with potassium. It was synthesized from metaiodophenol and potassium by Koerner [2] in 1868. Resorcinol is a member of the phenol group, with the chemical formula $C_6H_6O_2$; it is a metadihydroxybenzene.

orthodihydroxybenzene pyrocatechin — metadihydroxybenzene resorcinol — paradihydroxybenzene hydroquinone

The other members of the phenol group, pyrocatechin and hydroquinone, are too toxic for therapeutic use. The melting point of the colorless resorcinol crystals is 118 C., and the boiling point is 274 C. Resorcinol is readily soluble in water, alcohol, ether and fats.

Resorcinol was introduced into dermatotherapy by Andeer [3] in 1884, who credited it with a keratolytic action similar to that of salicylic acid. It was, however, primarily used as a strong caustic agent by this and other authors for tuberculous and syphilitic ulcers. Unna [4] was enthusiastic about its action and classified it as a reducing agent, stating that its reducing action should be grouped between that of sulfur and ichthammol on the one side and of pyrogallol and chrysarobin on the other. He [5] expressed the belief that all substances which have a strong affinity for oxygen or are capable of withdrawing oxygen from the tissues promote keratinization. Since resorcinol, especially in an alkaline solution, possesses a strong affinity for oxygen, it acts as a reducing agent. The hydrogen ion concentration of a 1 per cent aqueous solution is 4.97, and that of a 2 per cent concentration is 4.45 according to Perutz and Lustig.[6]

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The fifth condensed part of a thesis submitted to the faculty of the Graduate School of the University of Minnesota in partial fulfilment of the requirements for the Degree of Doctor of Philosophy in Dermatology and Syphilology.

1. Kellogg, J. C.: Ueber das Resorzin in der Dermatotherapie, Monatsh. f. prakt. Dermat. **24**:233, 1897.

2. Koerner, cited by Kellogg, J. C.: Ueber das Resorzin in der Dermatotherapie, Monatsh. f. prakt. Dermat. **24**:233, 1897.

3. Andeer: Das Resorzin in seiner Anwendung bei Hautkrankheiten, Monatsh. f. prakt. Dermat. **3**:141, 1884.

4. Unna, P. G.: (*a*) Ichthyol und Resorcin, Monatsh. f. prakt. Dermat., 1886, supp. 2: (*b*) Ichthyol und Resorcin, Hamburg, Leopold Voss, 1886.

5. Unna, P. G.: Ueberhautung und Ueberhornung, Berl. klin. Wchnschr. **35**:533, 1883.

6. Perutz, A., and Lustig, B.: Ueber die Wasserstoffionenkonzentration der in der Dermatologie verwendeten offizinellen Umschlagwasser, Arch. f. exper. Path. **149**:321, 1930.

Unna postulated the theory that resorcinol in a low concentration acts as a keratoplasticum while in a high (10 to 50 per cent) concentration it has a keratolytic effect. Samberger,[7] influenced by Unna's work, stated that 1 per cent resorcinol in water is capable of bringing about a keratoplastic effect and recommended it for the treatment of acute eczema.

The first experimental work with resorcinol was done by Kellogg [8] in Unna's laboratory in 1897. He applied 50 per cent resorcinol in alcohol to the ear of a rabbit and 20 per cent resorcinol in collodion to the ear of a guinea pig and to the skin of his own forearm. In the various experiments the number of the applications varied from twice daily for two days to once daily for fourteen days. He performed a total of eight experiments and concluded from his histologic sections of excised specimens of skin that the action of resorcinol is primarily keratolytic. It first produces a superficial necrosis which eventually leads to the exfoliation of the stratum corneum. He was unable to observe any changes in the cutis.

Saalfeld [9] recommended 10 per cent resorcinol in alcohol for the treatment of warts, and Ehrmann [10] lauded it for its bactericidal and soothing effect and recommended a 3 per cent concentration for keratoplastic effect, a 10 to 15 per cent concentration for keratolytic effect and a 30 per cent concentration for caustic effect. Taubert,[11] von Bueltzingsloewen [12] and Beer [13] used resorcinol as an anhidrotic with good results. Schaeffer [14] recommended 40 per cent resorcinol in alcohol for inflammatory lesions of the skin and furuncles. Jansion and Marceron [15] found resorcinol useful as an antiphotocatalyst in treatment of dermatosis due to light; they gave daily doses of 0.25 Gm. by mouth. Urbach and Konrad [16] used it topically for the same purpose.

EXPERIMENTAL STUDIES

Resorcinol was incorporated in the strength of 1, 3, 5, 10 and 15 per cent in the following bases: (1) petrolatum; (2) petrolatum and hydrous wool fat in equal parts; (3) a base consisting of 6 per cent of a group of esters and alcohols of cholesterol (chiefly oxycholesterol) in an aliphatic hydrocarbon (petrolatum) base [17]; (4) a base consisting of oleic acid, white petrolatum, oleic acid esters and amides of diethanolamine [18]; (5) a base containing stearyl alcohol 10.0 Gm., liquid

7. Samberger, F.: Eine neue Behandlung des akuten Eczems, Dermat. Wchnschr. **59**:899, 1914.

8. Kellogg, J. C.: Ueber das Resorcin in der Dermatotherapie: Histologische Untersuchungen der Einwirkung desselben auf die gesunde Haut, Monatsh. f. prakt. Dermat. **24**:233, 1897.

9. Saalfeld, E.: Ueber Warzenbehandlung, Med. Klin. **50**:1937, 1911.

10. Ehrmann, S.: Das Resorcin in der Dermatotherapie, Wien. med. Wchnschr. **71**:582, 1923.

11. Taubert: Resorcin-Percutol, ein neues Antihidroticum, München. med. Wchnschr. **71**:1117, 1924.

12. von Bueltzingsloewen: Resorcin-Percutol, München. med. Wchnschr. **71**:256, 1924.

13. Beer, A.: Resorcin-Percutol, Deutsche med. Wchnschr. **51**:1664, 1925.

14. Schaeffer, J.: Experimentelle Untersuchungen über den Einfluss der lokalen Behandlung auf die Entzündungen, Berl. klin. Wchnschr. **47**:886, 1910.

15. Jansion and Marceron: Le "corps lumiere" aeridinique. Son traitment preventif par la resorcine, Bull. Soc. franç. de dermat. et syph. **32**:358, 1925.

16. Urbach, E., and Konrad, J.: Ueber die durch den langwelligen Anteil des Sonnenspektrums erzeugte Lichtdermatosen, Strahlentherapie **32**:193, 1929.

17. The preparation was aquaphor, manufactured by the Duke Laboratories, Stamford, Conn.

18. The preparation used was hydrosorb, manufactured by the Abbott Laboratories, North Chicago, Ill.

petrolatum 10.0 cc., water 10.0 cc. and light petrolatum 70.0 Gm., and (6) a base containing zinc oxide 7.5 Gm., talc 7.5 Gm. and enough petrolatum to make 30.0 Gm. The technic used was previously described.[17]

The histologic changes observed are briefly summarized as follows: Swelling and formation of lacunas in the stratum corneum occur, which eventually lead to a separation of the lamellas and finally to keratolysis. A thickening of the stratum corneum is not uncommon. There is a decided intercellular and intracellular edema in the stratum granulosum and the stratum spinosum which leads to vesicle formation in the epidermis, often at a time when the stratum corneum is still adherent. There are signs of cellular necrosis in the stratum spinosum. The chromatic structure in the nucleus of the cells of the stratum granulosum and stratum spinosum is often absent, or the arrangement of chromatin is irregular. New formation of cells begins in the deeper layers, which leads to acanthosis. The newly formed cells, pushing upward, eventually lift up the superposed necrotic masses in the form of a scale. There is a decided papillary edema which almost always extends into the upper third of the stratum texticulare. This edema formation, which was seen as early as forty-eight hours after the application of 1 per cent resorcinol, is in sharp contrast to the findings of Kellogg,[8] who made a special point of its conspicuous absence. The vessels in the stratum papillare are dilated and often surrounded by lymphocytes, plasma cells and eosinophils. This is also contrary to Kellogg's findings.

These changes were always present, though the intensity of the process and the time necessary to produce them were dependent on the concentration of resorcinol and the ointment base in which it was applied.

COMMENT

Resorcinol was introduced as a keratolytic agent in dermatotherapy twenty-one years after its discovery (1863), at a time when the keratolytic action of salicylic acid was just being accepted by the medical profession and when it received wide attention by various investigators (for references to the literature see article by Kellogg[1]). While many experimental studies were made with salicylic acid, resorcinol was somewhat neglected. It was ranked second to salicylic acid in its use as a keratolyticum. It remained in the background, in spite of the early investigations by Unna[4] and Kellogg,[8] who praised its keratoplastic and keratolytic action. It should always stay there, as will be pointed out later.

I was unable to find any experimental study in which the action of resorcinol has been compared with that of salicylic acid. Kellogg was the only investigator, to my knowledge, who made histologic investigations of the action of resorcinol. He concluded from eight experimental studies, of which six were made on animal and only two on human skin, that one of the remarkable features of its action is the conspicuous absence of inflammatory changes in the cutis. This is contrary to all my observations. The outstanding and universal findings in this study were papillary edema, edema in the upper part of the cutis, vascular dilatation and perivascular round cell infiltration, all of which are inflammatory changes. Thickening of the stratum corneum and occasional parakeratosis were observed after the application of 1 to 3 per cent concentrations of resorcinol. These could be interpreted as keratoplastic changes. All other changes pointed rather to severe irritation, such as a decided intercellular and intracellular edema, leading to vesicle formation in the stratum corneum, which was frequently observed at a time when the keratolysis was only partial. The relation of the concentration of resorcinol in various bases to the onset of the keratolytic effect is shown in figure 1. Figure 2

shows for comparison the effect of the corresponding concentration of salicylic acid in identical bases.

It is obvious from these charts that the keratolytic action of resorcinol is inferior to that of salicylic acid. Similar to the previous findings with salicylic acid or sulfur,[19] a decided difference in the effect of resorcinol in the various bases was observed. The relation between concentration and time necessary to produce keratolytic changes is identical with that found in the studies on salicylic acid and sulfur.[19] Doubling the concentration of resorcinol shortens the time which is necessary to produce keratolysis but does not reduce it to half. Ten and 15 per cent concentrations gave results identical for all practical purposes.

The results of these studies indicate not only that the keratolytic effect of salicylic acid (in identical concentration and corresponding bases) is better than that of resorcinol but that the latter is far more irritating. This irritating property has long been recognized and due warning has been voiced in the literature. Bloch [20] spoke of severe eczematous reactions following the use of locally applied resorcinol, which he believed are group reactions of the dihydroxybenzene group. Cases of hypersensitivity to resorcinol have been reported by Urbach,[21] Almkvist,[22] Strandberg,[23] Nathan and Stern [24] and Katzenellenbogen.[25] Mitchell [26] reported

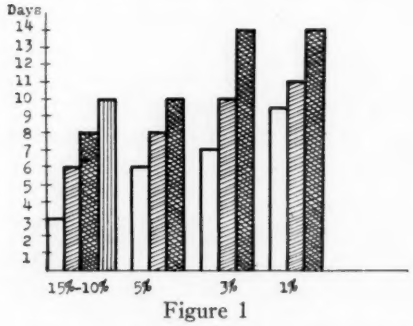

Figure 1

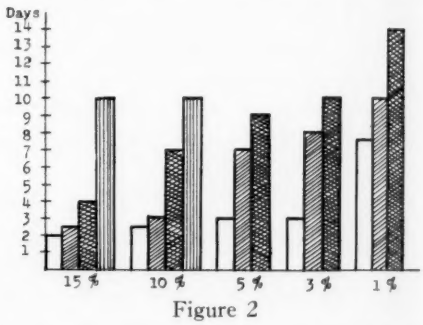

Figure 2

Fig. 1.—Beginning of the keratolytic action of resorcinol, as observed by histologic studies. Each bar indicates the average of four experiments. The blank bars indicate the oxycholesterol-petrolatum ointment base, the base consisting of fatty acid esters of diethanolamine in petrolatum and the base containing stearyl alcohol in liquid petrolatum, water and petrolatum; the bars with the diagonal lines, the petrolatum and hydrous wool fat base; the bars with crisscross lines, petrolatum, and the bars with vertical lines, zinc oxide paste. The same bases were used throughout all experiments.

Fig. 2.—Beginning of the keratolytic action of salicylic acid.

19. Strakosch, E. A.: (*a*) Studies on Ointments: Penetration of Various Ointment Bases, J. Pharmacol. & Exper. Therap. **78**:65, 1943; (*b*) Studies on Ointments: II. Ointments Containing Salicylic Acid, Arch. Dermat. & Syph. **47**:16 (Jan.) 1943; (*c*) Studies on Ointments: III. Ointments Containing Sulfur, ibid. **47**:216 (Feb.) 1943.

20. Bloch, B.: Pathogenese, Arch. f. Dermat. u. Syph. **145**:77, 1934.

21. Urbach, E.: Ueberempfindlichkeit gegen Körper der Dioxybenzolgruppe, besonders gegen Resorcin, Zentralbl. f. Haut- u. Geschlechtskr. **12**:243, 1924.

22. Almkvist, J.: Vergiftung bei äussere Anwendung von Resorcin, Zentralbl. f. Haut- u. Geschlechtskr. **23**:167, 1927.

23. Strandberg, J.: Foergiftning vid utvaertes bruk av resorcin, Svenska läk.-tidning. **24**:276, 1927.

24. Nathan, E., and Stern, F.: Chemische Analyse der Hautüberempfindlichkeit bei einem Fall von Resorcinidiosynkrasie, Dermat. Wchnschr. **40**:1471, 1930.

25. Katzenellenbogen, I.: Concerning Hypersensitivity to Resorcin, Urol. & Cutan. Rev. **43**:466, 1939.

26. Mitchell, J. H.: Resorcin Anal Dermatitis Due to Resorcin in Anusol Suppositories, J. A. M. A. **101**:1067 (Sept. 30) 1933.

a severe anal dermatitis following the use of suppositories containing resorcinol. Templeton [27] observed cheilitis following the use of a toothpaste which contained resorcinol and severe dermatitis in a patient who used a hair tonic which contained 5 per cent resorcinol in alcohol.

According to Ellinger [28] toxic manifestations, such as vomiting, dyspnea, cyanosis, petechiae, delirium and even death, following the topical application of resorcinol are due to the formation of methemoglobin. Such incidents have been

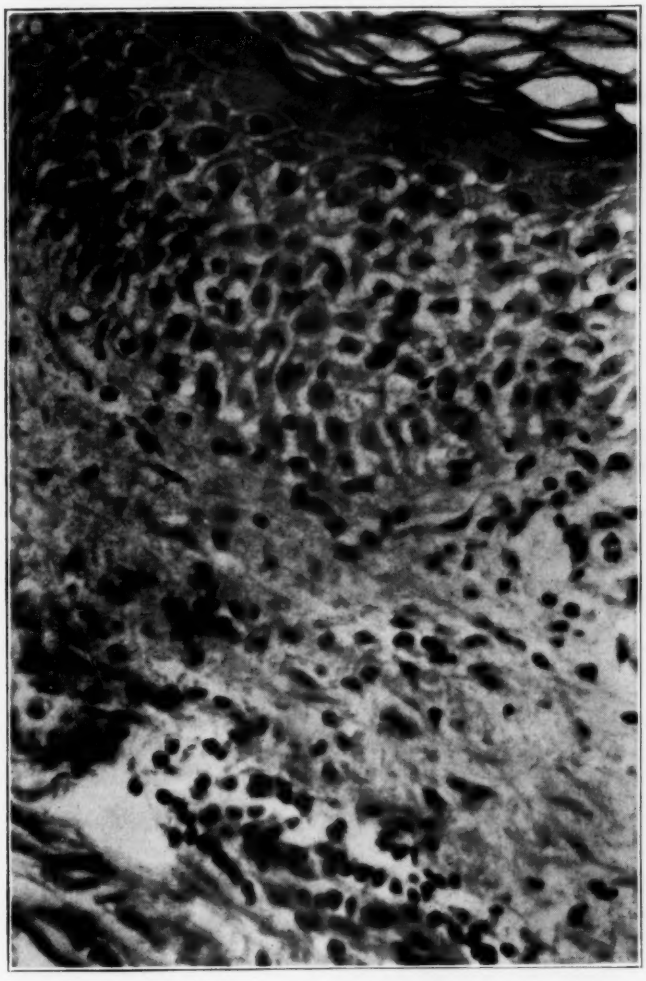

Fig. 3.—The effect of 5 per cent resorcinol in a base consisting of fatty acid esters of diethanolamine in petrolatum after three days of application. Note the heavy intercellular and intracellular edema, cell necrosis in stratum spinosum.

observed by Strandberg,[23] Boeck,[29] Connerth [30] and Flandin, Rabeau and Ukrainczyk.[31]

27. Templeton, H. J.: Cheilitis and Dermatitis from Resorcinol and a Derivative, Arch. Dermat. & Syph. **42**:138 (July) 1940.

28. Ellinger: Aromatische Kohlenwasserstoffe, in Heffter, A.: Handbuch der Experimentellen Pharmakologie, Berlin, Julius Springer, 1923, vol. 1.

(Footnotes continued on next page)

Children appear to be more sensitive than adults to resorcinol. Kyrle [32] warned against its local use for children, even with intact skin. Nothen [33] reported the case of an 11 day old infant to whose skin 3 per cent resorcinol in petrolatum was applied; the child became restless and cyanotic shortly thereafter and died twenty-four hours later. Murray [34] in an analysis of 60 cases of drug poisoning in children reported 4 fatalities due to resorcinol. Haenelt's [35] patient died shortly after the application of 5 per cent resorcinol in petrolatum. A similar case was reported by

Fig. 4.—The effect of 10 per cent resorcinol in petrolatum and hydrous wool fat (equal parts) after ten days. Beginning of exfoliation and large vesicle formation, edema in the cutis and round cell infiltration are shown.

29. Boeck, C.: Fall von tödlicher Resorcinvergiftung bei äusserer Anwendung des Mittels, Dermat. Wchnschr. **60**:449, 1915.

30. Connerth, O.: Die Anwendung des Resorcins und seine Schädigungen im Kindesalter, Ztschr. f. Kinderh. **39**:628, 1925.

31. Flandin, C. H.; Rabeau, H., and Ukrainczyk: Intolérance à la resorcin, Bull. Soc. franç. de dermat. et syph. **42**:1804, 1925.

Liebenam,[36] and one can safely assume that there were many more cases observed which were not reported.

I have not encountered fatalities from resorcinol but have observed numerous examples of irritation following its topical use. The number of reported irritations, toxic manifestations and fatalities following the topical use of the drug in question is alarming, if one considers how relatively little it is used. While I am unable to give any figures of how much resorcinol is used locally in a year in any country, many pharmaceutic firms have communicated to me that the amount of resorcinol used in a year's time is almost negligible compared with their estimated amount of salicylic acid used for topical application. It is realized that the estimated figures are at best only guesses, but the amount of salicylic acid used in topical application must certainly be and probably always has been considerably higher than the amount of resorcinol used. There has been to my knowledge, however, only one reported fatality from the local use of salicylic acid.[37]

Considering all this and assuming for the moment that the keratolytic action of salicylic acid and that of resorcinol were equal, one would certainly choose the former. However, not only is resorcinol more irritating but its keratolytic action is considerably inferior to that of salicylic acid and its keratoplastic action is less than that of sulfur, which is also less irritating. Thus there is no advantage in the use of resorcinol.

SUMMARY

1. The literature on the topical use of resorcinol has been reviewed.

2. Resorcinol was incorporated in the strength of 1, 3, 5, 10 and 15 per cent in the following bases: (1) petrolatum; (2) equal parts of petrolatum and hydrous wool fat; (3) an oxycholesterol-petrolatum ointment base; (4) fatty acid esters of diethanolamine in petrolatum; (5) stearyl alcohol in liquid petrolatum, water and petrolatum, and (6) zinc oxide in talc and petrolatum. Biopsies were performed after one, two, three, seven, ten and fourteen days, and the keratolytic action of these ointments on normal human skin was studied histologically.

3. The keratolytic action of resorcinol was compared with that of salicylic acid, in identical concentrations and bases. It was found that it is not only more irritating than salicylic acid but its keratolytic action is inferior to that of salicylic acid.

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32. Kyrle, J.: Beiträge zur Kenntnis der Resorcinvergiftung bei äusserer Anwendung des Mittels, Dermat. Ztschr. **22**:505, 1915.

33. Nothen, H.: Ueber Resorcinvergiftung bei äusserer Anwendung, Med. Klin. **24**:901, 1908.

34. Murray, L. M.: An Analysis of Sixty Cases of Drug Poisoning, Arch. Pediat. **43**:193, 1926.

35. Haenelt, M.: Ein Fall von perkutaner Resorcinvergiftung, München. med. Wchnschr. **72**:386, 1925.

36. Liebenam, L.: Ueber Resorcinvergiftung im Säuglingsalter, Med. Welt **9**:1217, 1935.

37. Sannicandro, G.: Morte inopinata da applicazione di pomata salicilica (studio clinico ed anatomo-patologica e contributo alla conoscenza della cosidetta "acidosi salicilica"), Dermosifilografo **12**:273, 1937.

VITILIGO

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AND
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Lesions of vitiligo differ from normal skin by the inability of their melanoblasts to form melanin pigment in response to pigmentogenic stimuli. This inability is complete in spite of the presence of melanoblasts [1] and is demonstrated microscopically by a negative dopa reaction.[2] The question whether depigmented skin in vitiligo differs from normal skin also in other respects is not settled. Inconsistent and often contradictory observations have been made about this problem.

Königstein [3] found that there is decreased perception of touch, pain and temperature in vitiliginous spots, but others found that such hypoesthesia is not restricted to the depigmented areas and has nothing to do with the pigmentary disturbance.[4] Autonomic nervous reflex impulses, such as pilomotor, vasomotor and mamillary reflexes, have been said to be modified in vitiligo.[5] These observations, however, lack confirmation.

Decreased secretion of sweat in depigmented spots in vitiligo in response to pilocarpine was found by several authors; the literature of this topic was reviewed by Habermann.[4]

The question as to whether the inflammatory responses of depigmented skin to chemical stimuli are increased, decreased or normal was often discussed. Here again the observations are controversial, as can be seen from the reviews of Pillsbury and Kulchar [6] and Habermann [4] on this topic. Observations on increased absorptiveness [7] and on decreased autolysis in nonpigmented skin [8] remain unconfirmed.

In the present communication an observation will be reported which was first thought to be an indication of an abnormal responsiveness of depigmented skin independent of the pigmentary disturbance. However, the final analysis of

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From the Section of Dermatology, Department of Medicine, University of Chicago.

1. Becker, S. W.: Vitiligo: A Clinical and Histologic Study, with a Consideration of Pinta, Arch. Dermat. & Syph. **28**:497-507 (Oct.) 1933.

2. Bloch, B.: Das Pigment, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1927, vol. 1, pt. 2, pp. 431-541.

3. Königstein, H.: Sensibilitätsstörung bei Vitiligo, Wien. klin. Wchnschr. **23**:1745-1748, 1910.

4. Habermann, R.: Vitiligo, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1933, vol. 4, pt. 2, pp. 896-930.

5. Lévy-Franckel, A., and Juster, E.: Vitiligo avec troubles nerveux sensitifs et sympathiques; l'origine sympathique du vitiligo, Bull. Soc. franç. de dermat. et syph. **28**:338-342, 1922. Lévy-Franckel, A.; Guillaume, A. C., and Juster, E.: Examen de la circulation cutanée dans la pélade et vitiligo, ibid. **32**:342-345, 1925.

6. Pillsbury, D. M., and Kulchar, G. V.: Gold Dermatitis Limited to Depigmented Skin, with a Theoretical Consideration of Its Etiology, Arch. Dermat. & Syph. **27**:36-48 (Jan.) 1933.

7. Königstein, H.: Reaktionsunterscheide zwischen gefärbter und ungefärbter Haut, Arch. f. exper. Path. u. Pharmakol. **97**:262-271, 1923.

8. Blazsó, S.: Autolysis of Pigmented and Non-Pigmented Skin, Magyar orvosi arch. **32**:209-219, 1931.

the phenomenon led to the conclusion that the observed anomaly is a remote and unexpected consequence of the lack of melanin pigment in vitiligo.

EXPERIMENTAL WORK

1. Experiments with Ferrous Salts.—In the last fifteen years much attention has been paid to the possible role of heavy metals in the process of melanin formation. Animal experiments showed a lower content of copper in areas of nonpigmented skin than in pigmented skin. The literature on this problem was thoroughly reviewed by B. Schaffer.[9] Attempts have been made to utilize for therapeutic purposes the catalytic effect of heavy metals in pigment formation. General[10] and local[10b] administration of gold compounds were claimed to be effective in the therapy of vitiligo, whereas the local application of copper and copper salts in combination with ultraviolet radiation was reported to be without any effect.[9]

We were impressed by the powerful catalytic effect which small amounts of ferrous salts exerted on the oxidation of tyrosine solutions by ultraviolet rays in vitro.[11] It seemed that in the presence of ferrous salts ultraviolet radiation might easily produce melanin from tyrosine or from its derivatives in the tissues, in spite of the absence of the otherwise necessary oxidative enzyme. Therefore we tried to introduce ferrous salts into the epidermis by various methods. Among them the electrophoretic introduction was tested by applying aqueous solutions of ferrous sulfate and ferrous ammonium sulfate to the skin from the positive pole of a galvanic current. It is known[12] that by such arrangement cations of electrolytes are transported through the follicular pores and ducts of the sweat gland toward the capillary vessels under the influence of the electric current. If the intensity is high enough and the electrophoresis is prolonged, it may happen that the electrically transported cations break through the side wall of the follicle into the surface epidermis and into the upper layers of the corium.[13a] Thus one may impregnate the basal layer of the epidermis around the follicles with ferrous ions, as shown in figure 3. We have not succeeded as yet in obtaining pigmentation by such impregnation followed by ultraviolet irradiation. However, during these experiments a peculiar observation was made.

In the first experiment a 1 per cent aqueous solution of ferrous sulfate was introduced from the positive pole with an electric intensity of 1 milliampere per square centimeter on the extensor side of the upper part of the right arm of a normal person. Immediately after the removal of the electrodes punctate brown spots were seen in the treated area at the site of the follicular pores. This discoloration persisted for three weeks.

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9. Shaffer, B.: The Effect of Copper in Vitiligo, J. Invest. Dermat. **1**:225-234, 1938.

10. (*a*) Lindsay, H. C. L.: Treatment of Leukoderma with Gold Sodium Thiosulfate, Arch. Dermat. & Syph. **20**:22-26 (July) 1929. (*b*) Yang, K. L.: The Treatment of Vitiligo with Intradermal Administration of Gold, Acta dermat.-venereol. **21**:657-666, 1940.

11. Rothman, S.: In Vitro Studies on Pigmentation, J. Invest. Dermat. **5**:61-75, 1942.

12. Rothman, S.: Resorption durch die Haut, in Bethe, A.; von Bergmann, G.; Emden, G., and Ellinger, A.: Handbuch der normalen und pathologischen Physiologie mit Berücksichtigung der experimentellen Pharmacologie, Berlin, Julius Springer, 1929, vol. 4, pp. 107-151; 1932, supp. 18, pp. 85-91.

13. (*a*) Rein, H.: Zur Electrophysiologie der menschlichen Haut, Ztschr. f. Biol. **84**:41-50, 1926. (*b*) Abramson, H. A., and Gorin, M. H.: Skin Reactions: IX. The Electrophoretic Demonstration of the Patent Pores of the Living Human Skin; Its Relation to the Charge of the Skin, J. Physiol. Chem. **44**:1094-1102, 1940. (*c*) Abramson, H. A., and Engel, M. G.: Skin Reactions: XII. Patterns Produced in Skin by Electrophoresis of Dyes, Arch. Dermat. & Syph. **44**:190-200 (Aug.) 1941.

Similar "pore patterns" were reported earlier to have followed electrophoretic introduction of positively charged aniline dyes.[13]

In twenty following experiments on the normal skin of 13 persons it was found that such a pattern appeared, without exception, after the electrophoresis of ferrous sulfate and ferrous ammonium sulfate in aqueous and in 50 per cent alcoholic solutions. In these twenty experiments the concentration of the solution varied from 0.05 to 2 per cent, the duration of the treatment from five to thirty minutes and the intensity of the current from 0.5 to 2.5 milliamperes per square centimeter of area.

It was found that if the time of exposure was short or the intensity was low or the solution was highly dilute the "pore pattern" appeared not immediately

Fig. 1.—Lack of "pore pattern" in vitiligo after electrophoretic introduction of ferrous sulfate. The outer mark delineates the site of the electrode. The diagonal line marks the border of the pigmented and depigmented areas.

after treatment but after a more or less prolonged latent period. In one instance, for example, a 0.1 per cent solution of ferrous sulfate was introduced with 1 milliampere intensity per square centimeter for only five minutes. The "pore pattern" appeared five hours later. It was further observed that under such mild experimental conditions the "pore pattern" gradually became more intense, particularly in the first twenty-four hours.

The "pore pattern" persisted from several days to six months. Its duration was to a certain degree proportional to the intensity of treatment. However, the duration of the pattern was also influenced by the intensity and speed of desquamation. If the electric current elicited slight inflammation with clinically manifest postinflammatory desquamation, the duration of the pattern was shorter than if such increased desquamation did not occur.

The same type of procedure was then carried out in thirteen experiments on 10 patients with vitiligo. The positive electrode was applied to the skin so that one half of the ferrous salt solution fell on depigmented and one half on normal skin.

It was found that vitiliginous skin did not display any "pore pattern." At the most, a few discolored follicular pores were visible, whereas the surrounding pigmented skin showed a normal behavior (figs. 1 and 2). The same observation

Fig. 2.—Lack of "pore pattern" in vitiligo after electrophoretic introduction of ferrous sulfate. Close view.

was made on 1 patient with postarsenical spotted melanosis and leukoderma. In the leukoderma spots which were dopa negative no "pore pattern" developed. There was only one exception, in an area of recent vitiligo, where a "pore pattern" identical with that of the surrounding pigmented skin developed. Older vitiliginous lesions of the same patient did not show any "pore pattern." We had no opportunity to make a biopsy on the spot of recent vitiligo, and thus it could not be stated whether it was completely dopa negative.

The absence of "pore pattern" in vitiligo could be explained on an anatomic basis if it were shown that follicles are lacking or are scarcer in vitiliginous than in pigmented skin. Such an anomaly was not reported previously, however, and our own histologic preparations did not substantiate such a possibility.

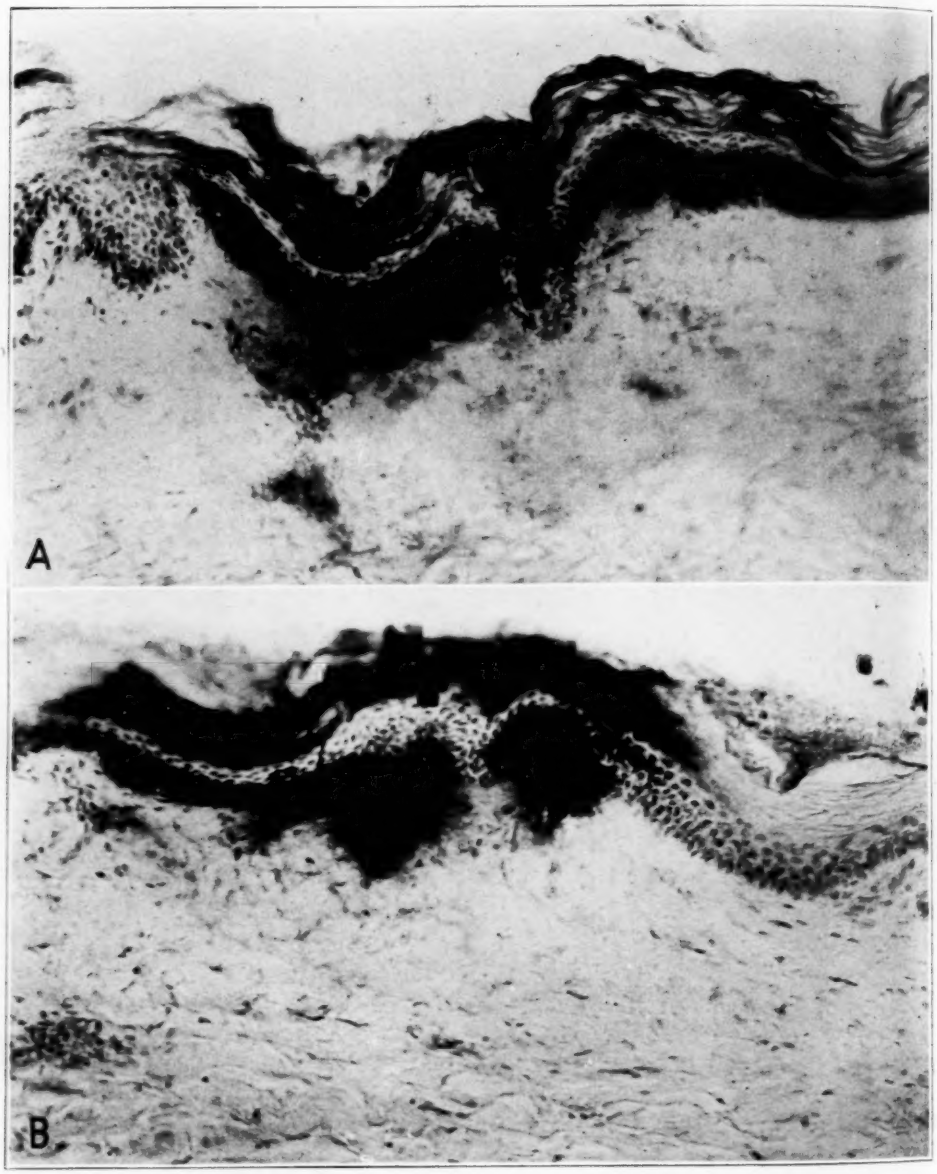

Fig. 3.—*A*, pigmented area; *B*, depigmented area on the right side. The permeation of iron into follicles and perifollicular tissue is about equal in the two areas.

Four biopsies were made at the boundary between the normal and the depigmented skin after the electrophoretic experiments, and the microscopic sections were subjected to the iron stain method in the modification of Gömöri.[14] Sur-

14. Gömöri, G.: Microtechnical Demonstration of Iron, Am. J. Path. **12**:655-663, 1936.

prisingly, in these sections no definite differences were found between the iron content of the infundibula of depigmented and of pigmented parts. Pores within the depigmented spots, which clinically did not show any discoloration, and pores within the pigmented skin, which were dark brown, were equally loaded with iron (fig. 3). If there were differences, they were far too inconclusive to explain the striking macroscopic differences.

This observation suggested that the differences in "pore pattern" must be based on a different chemical behavior of the surfaces of the pores. It was assumed that ferrous ions enter the pores in both vitiliginous and pigmented skin but that in the pores of pigmented skin the ions undergo a chemical change which leads

Fig. 4.—Application of a 5 per cent solution of silver nitrate on a square of filter paper to the upper patch of vitiligo and the surrounding pigmented skin. The treated lesion does not show any darkening; its color is identical with that of the untreated lower patch of vitiligo. The pigmented part of the treated area is considerably darkened.

to the precipitation of some brown substance, possibly metallic iron, whereas the vitiliginous pores do not elicit such a chemical reaction. The validity of this assumption was proved in experiments with silver nitrate on the basis of Woronoff's work.[15]

2. Experiments with Silver Nitrate.—In 1930 Woronoff [15] reported the following experiment: A strip of filter paper was soaked in a 5 per cent solution of silver nitrate and then placed across a depigmented spot and the pigmented

15. Woronoff, D. L.: Die Silberreaktion an der Hautoberfläche bei Vitiligo und bei anderen Pigmentationsstörungen. Reflexionen über die erhöhte, wie herabgesetzte Sensibilität bei Vitiligo, Dermat. Wchnschr. **90**:105-111, 1930.

neighboring area on the skin of a patient with vitiligo. This strip was left on the skin for five to eight minutes, during which time it was repeatedly moistened with the silver nitrate solution. It was then removed, and the pigmented skin appeared considerably darkened, whereas the depigmented skin did not show any change of color.

This experiment was repeated in our laboratory four times on 3 patients with vitiligo, with the same result as reported by Woronoff (fig. 4). Also in agreement with Woronoff, we found that such an experiment had to be carried out in subdued light so that an immediate photochemical reduction of silver nitrate to silver would not occur. If there was an intense photochemical action, a layer of metallic silver was deposited on the depigmented skin. However, when carried out in subdued light, the experiment clearly demonstrated that the surface of the pigmented skin took active part in the reduction of silver nitrate whereas the surface of depigmented spots did not.

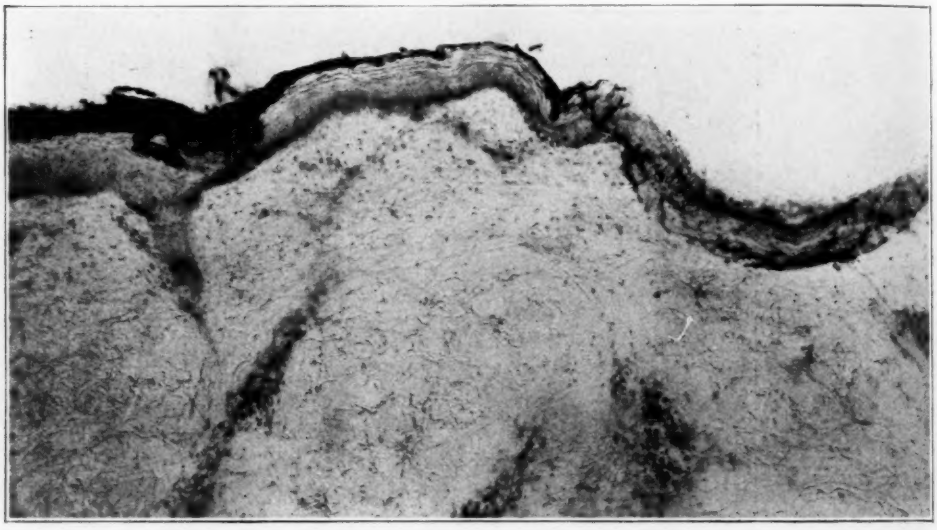

Fig. 5.—Application of a 5 per cent solution of silver nitrate to normal skin in vivo. At the border of application the silver nitrate permeates only the most superficial lamellas of the horny layer.

Subsequently, the silver nitrate experiment was repeated on a normal brunette with an average degree of pigmentation, and a biopsy was made on tissue from the border between the untreated and the treated skin. Immediately after the tissue was removed frozen sections were made, and it was seen in the microscopic sections that the darkening of pigmented skin after local application of silver nitrate solution was due to a discoloration of only the horny layer. As shown in figure 5, silver nitrate not only did not penetrate into the epidermis but did not even impregnate the whole thickness of the horny layer over the entire area. It was concluded that the superficial horny lamellas in pigmented skin were chemically different from the corresponding lamellas of depigmented spots, as the latter did not show discoloration after treatment with silver nitrate. The horny layer of pigmented skin reduced silver nitrate; the horny layer of depigmented spots did not.

Woronoff [15] assumed that some "decomposition products" of melanin are carried up into the horny layer in pigmented skin and that these products are responsible for the reducing action of the horny layer. However, he did not present any evidence for this supposition.

From 2 of our patients with vitiligo and from 1 patient with postinflammatory leukoderma, biopsy specimens were taken in border areas, and frozen sections were prepared and treated with a 10 per cent solution of silver nitrate for five minutes and then lightly stained with alum-hematoxylin solution. These sections when examined under low power (fig. 6) showed clearly that the horny layer of the pigmented part of the section was deeply darkened by the silver nitrate treatment whereas the horny layer of the vitiliginous part was not. At examination under high power (fig. 7) a fine pigment dust could be seen in the horny layer over the pigmented areas. Also it could be seen that this dust originates in the melanin granules in the basal layer and is carried to the horny layer by the daughter cells of the stratum Malpighii. The dusty precipitate in the horny layer is densest above the tips of the papillae, from which points the pigment granules of the basal layer have to be transported a considerably shorter distance

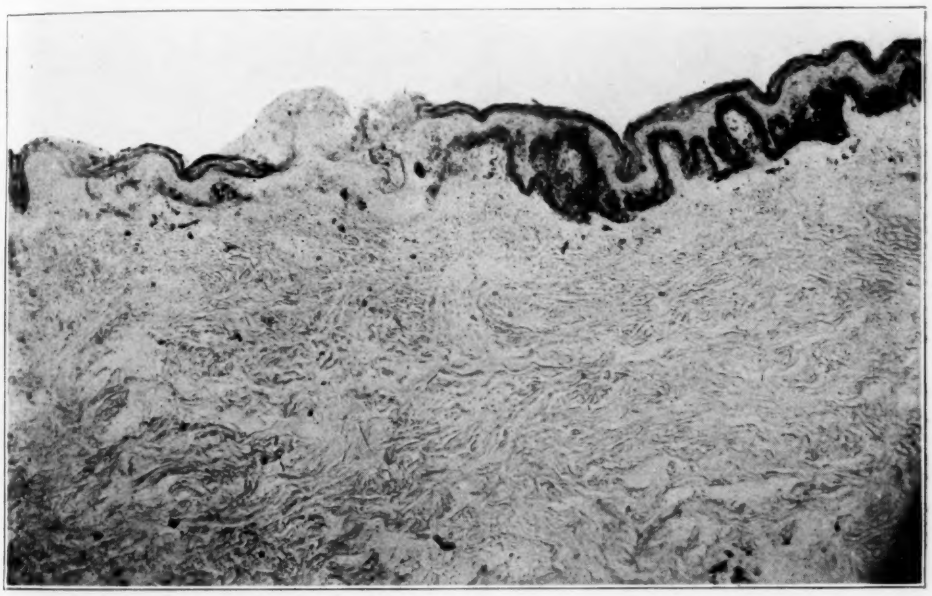

Fig. 6.—Border area of vitiligo treated with silver nitrate in vitro. Darkening of the horny layer is seen only above the pigmented epidermis.

to reach the horny layer than from the points in between the papillae (figs. 6 and 7). Above the interpapillary pegs the pigment dust in the horny layer is definitely scarcer than above the papillary tips. No pigmentary dust whatsoever was seen in the horny layer of the vitiliginous parts (fig. 6).

It is well known that melanin granules darken considerably from treatment with silver salts because melanin reduces the salts to metallic silver and at the same time is oxidized to a darker product.[16] It is evident from figure 6 that the pigment dust in the horny layer becomes visible through darkening by the silver treatment, as do the granules in the basal layer.

We endeavored to measure the amount of silver nitrate which is reduced to metallic silver by horny scales of pigmented skin. The scales were scraped off from pigmented and depigmented skin. Equal amounts (4.5 mg.) of the scales of both types were weighed on the analytic balance. Both samples were transferred

16. Miescher, G., and Minder, H.: Untersuchungen über die durch langwelliges Ultraviolett hervorgerufene Pigmentdunkelung, Strahlentherapie **66**:6, 1939.

to small test tubes, and 0.5 cc. of a 1 per cent solution of silver nitrate was added to each. Both samples were homogenized by means of an all glass homogenizer. Five tenths cubic centimeters of the 1 per cent solution of silver nitrate was pipetted also into a third tube, which did not contain scales. The three tubes were placed in a dark incubator at 38 C. for thirty minutes, and the concentration of the silver ions was estimated by the colorimetric method of Bouilloux.[17] In the reaction described by Bouilloux the depth of the final color is proportionate to the concentration of silver ions. It was found that silver ions were used up by both

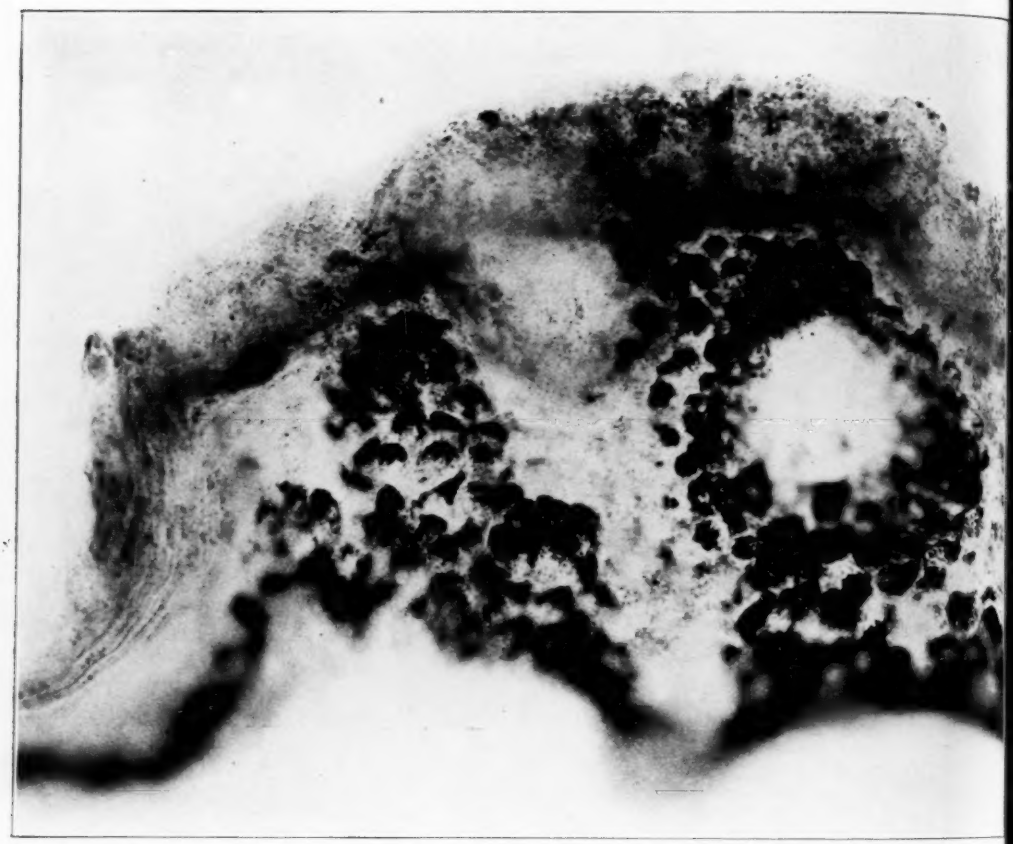

Fig. 7.—High power view of pigmented skin from figure 6. Melanin granules in the horny layer are particularly dense above tips of papillae.

types of scales in the same degree. The equal loss of silver ions was, however, considerable in both of the tubes containing scales.

Transmission of Light in Percentages

Solution of Silver Nitrate and Pigmented Scales	Solution of Silver Nitrate and Vitiligo Scales	Solution of Silver Nitrate
94	92	25

In a second experiment it was found that 4.5 mg. of both pigmented and nonpigmented scales removed completely the silver ions from 0.5 mg. of silver nitrate

17. Bouilloux, G.: Microchemical Detection and Determination of Silver and Mercury, Bull. Soc. chim. biol. **7**:184-187, 1940.

in ten minutes. The scales were suspended in 1 cc. of solution containing 0.5 mg. of silver nitrate.

Apparently, scales form silver proteinate complexes with silver nitrate. This rather intense process dominates and overshadows the comparatively small reducing effect of the pigment dust in the scales. At the present time this seems to be the best explanation for the failure to demonstrate by chemical methods the different behavior of pigmented and nonpigmented scales. This difference, however, is obvious from the histologic observations.

Woronoff [15] reported that scales scraped from normal skin darken visibly in silver nitrate solutions, whereas scales from vitiligo lesions do not. We were unable to duplicate this observation.

Additional Observations.—Before it became clear from microscopic examinations that the "pore pattern" was overwhelmingly a discoloration of the infundibula of the hair follicles and not of the pores of the sweat gland, we thought that lack of "pore patterns" in vitiligo might be due to a decreased function of sweat glands in the depigmented spots. Such an assumption was supported by earlier observations of decreased secretion of sweat in depigmented areas.[4] Ducts of nonfunctioning sweat glands are filled with air instead of sweat, and thereby the electric conductivity of these ducts is lowered.

Two methods were used to test the validity of our assumption. First, a series of measurements of cutaneous resistance were carried out by Darrow's behavior research polygraph [18] on depigmented and on neighboring skin of patients with vitiligo. These measurements did not show any consistent differences. Secondly, the sweating ability of depigmented and of neighboring pigmented skin in response to heat and to intradermal injections of acetylcholine was tested, the sweat secretion being visualized by Minor's iodine-starch method.[19] In two experiments heat was applied by means of an electric heat box to the arm of a patient with extensive vitiligo. In experiments on 3 patients with vitiligo 0.3 cc. of acetylcholine bromide in isotonic solution of sodium chloride (in a 1 : 1,000 concentration) was injected intradermally, as described by Kahn and Rothman.[20] We did not find the slightest difference between the sweating ability of depigmented and that of pigmented skin in response to either heat or acetylcholine.

The pilomotor response to intradermal injections of acetylcholine [21] also was equal in pigmented and depigmented skin.

In the electrophoretic experiments 2 of 10 patients with vitiligo voluntarily told us that during the galvanization they felt less burning in the vitiliginous spots than in the surrounding area. This observation seems to confirm the statement of Königstein [3] on decreased perception of pain in vitiligo.

COMMENT

We conclude that the "pore pattern" appearing after the electrophoretic introduction of ferrous sulfate into pigmented skin is due to the reduction of the ferrous ions to an insoluble brown product by the melanin particles of the superficial

18. Darrow, C. W.: Continuous Quantitative Records in Standard Units by the Wheatstone Bridge Method, J. Gen. Psychol. **4**:418-420, 1930.

19. Minor, V.: Ein neues Verfahren zu der klinischen Untersuchung der Schweissabsonderung, Deutsche Ztschr. f. Nervenh. **101**:302-308, 1927.

20. Kahn, D., and Rothman, S.: Sweat Response to Acetylcholine, J. Invest. Dermat. **5**:431-444, 1942.

21. Rothman, S., and Coon, J. M.: Pilomotor Action of Nicotine: A New Pharmacodynamic Test of the Skin, Arch. Dermat. & Syph. **40**:999-1000 (Dec.) 1939; Axon Reflex Responses to Acetylcholine in the Skin, J. Invest. Dermat. **3**:79-97, 1940.

horny lamellas. This interpretation, even though not based on direct evidence, is strongly suggested by the results of the experiments with silver nitrate and by the lack of "pore pattern" in vitiligo. That the reduction of silver nitrate is due to the melanin content of horny lamellas is evidenced by the fact that the horny layer of depigmented skin produces no such effect. Woronoff assumed that "decomposition products of melanin" are responsible for the reducing effect of the horny layer. It is obvious from our photomicrographs (fig. 7) that this explanation is correct if in place of the hypothetic "decomposition products" the expression "melanin dust" is substituted. There is no reason to assume that melanin is decomposed while being transported to the horny layer. From animal experiments it is known that melanin is cast off with the horny layer.[22]

In the electrophoretic experiments ferrous salts are taken up only by those horny lamellas which are situated around the follicular infundibula, because the electric transport goes through the follicles. Wherever ferrous ions enter the pigmented horny layer, they are reduced to a brown precipitate, probably metallic iron. If the horny layer is bare of pigment granules, as it is in lesions of vitiligo and leukoderma, such reduction does not take place, in spite of the fact that ferrous sulfate enters the pores in vitiliginous as well as in normal skin. This has been demonstrated in figure 3.

SUMMARY AND CONCLUSIONS

Electrophoretic introduction of ferrous salts into normally pigmented skin causes a brown discoloration of the follicular pores. This "pore pattern" does not appear in depigmented skin.

Local application of solution of silver nitrate to pigmented skin results in darkening of the superficial lamellas of the horny layer. Such discoloration is not seen in the horny layer of vitiliginous spots.

The reduction of silver nitrate by the horny layer in pigmented skin is due to the presence of fine melanin granules in the horny layer. Such granules are not present in vitiligo.

It is concluded that when ferrous salts are introduced electrophoretically the lack of "pore pattern" in vitiligo is due to the inability of the depigmented horny layer to reduce ferrous salts.

There is no difference between the sweating ability and pilomotor response of pigmented and those of depigmented skin.

Hypalgesia of the depigmented spots in vitiligo was observed in 2 of 10 patients.

Mr. John Muntz and Mr. Thomas Singer assisted in the chemical experiments on reduction of silver; Mr. Jonas Schreider assisted in the measurements of cutaneous resistance, and Dr. George Gömöri helped with the iron stain. The histologic part of this work was done with the technical help of Miss Dorothy Shaw.

950 East Fifty-Ninth Street.

22. Meyer, H.: Experimentelle Untersuchungen über den Abtransport des Hautpigments; Ein Beitrag zur Frage des Ursprungs des Cutispigments, Dermat. Ztschr. **32**:348-355, 1921.

Clinical Notes

A CASE OF KELOIDS OF UNUSUAL SIZE

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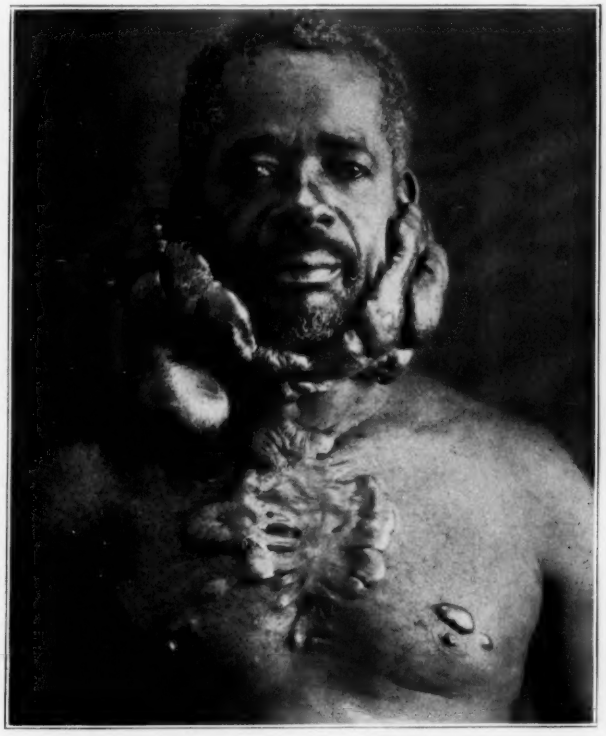
A case of keloids is herein reported on account of the unusual size and extent of the lesions.

REPORT OF CASE

D. D., a Negro aged 52, born in Brazil, was examined on May 30, 1939. The family and the personal history were irrelevant, there being no history of any cutaneous traumatism. The



Keloids of unusual size.

disease of the skin was first noticed twelve years previously as a small tumor in the mid-sternal region which gradually spread and enlarged to its present size. The lesions caused pruritus at night but no pain or tenderness. The patient had not received any treatment. A general physical examination showed nothing abnormal except the following changes in the skin:

There were large lobulated tumors on each side of the neck extending along the lower jaw and chin. The largest tumor was the size of an orange. These tumors were connected by a narrow band with a large, flat elevated area in the midsternal region of about 12 cm. in width. The borders showed pseudopod-like prolongations which were elevated and sharply

defined. Near the nipples were a few small isolated tumors. The disease involved the lobules of the ears. The back of the neck and the rest of the cutaneous surface were free of the disease. The lesions were all hard, smooth and purplish and devoid of pain or tenderness.

COMMENT

Keloids of unusual size and extent have been reported by Gromier,[1] Narducci,[2] Amicis,[3] Oliver,[4] Silva,[5] Fox,[6] Tzanck, Sidi and Armus,[7] Hertzler,[8] Eller,[9] Medeiros [10] and Becker and Obermayer.[11]

Rua Ceará, 1695.

1. Gromier, E.: Bull. Soc. path. exot. **20**:553-556, 1927.
2. Narducci, F.: Dermosifilografo **5**:145-156, 1930.
3. Amicis, T., cited by Woringer, F., in Darier, J.: Nouvelle pratique dermatologique, Paris, Masson & Cie, 1936, vol. 6, p. 564.
4. Oliver, E. A., in Ormsby, O. S.: Diseases of the Skin, ed. 5, Philadelphia, Lea & Febiger, 1937, p. 625.
5. Silva, F., cited by Nékám, L.: Corpus iconum morborum cutaneorum, Leipzig, Johann Ambrosius Barth, 1938, pt. 3, p. 701.
6. Fox, H., cited by Nékám, L.: Corpus iconum morborum cutaneorum, Leipzig, Johann Ambrosius Barth, 1938, pt. 3, p. 702.
7. Tzanck, A.; Sidi, E., and Armus, J.: Bull. Soc. franç. de dermat. et syph. **45**:1815-1818, 1938.
8. Hertzler, A. E., and Hollister, I. W., cited by Sutton, R. L., and Sutton, R. L., Jr.: Diseases of the Skin, St. Louis, C. V. Mosby Company, 1939, p. 647.
9. Eller, J. J.: Tumors of the Skin, Philadelphia, Lea & Febiger, 1939, p. 32.
10. Medeiros, O.: Brasil-med. **54**:56-58, 1940.
11. Becker, S. W., and Obermayer, M. E.: Modern Dermatology and Syphilology, Philadelphia, J. B. Lippincott Company, 1941, p. 590.

RESISTANT SYPHILIS (NONRESISTANT IN WIFE)

H. J. Templeton, M.D., Oakland, Calif.

Because of the possibility of some strains of Spirochaeta pallida being particulary virulent, I am reporting the following cases in which syphilis was extremely resistant to treatment in a man but followed a mild course when transmitted to his wife:

J. W. P., aged 30, a white man, was referred to me by Dr. Frank Baxter because of extensive mucous patches in his mouth and a widespread papular secondary eruption. He had had a penile lesion three months previously. The Wassermann reaction of the blood was strongly positive.

Eight weekly injections of mapharsen, 0.06 Gm., along with a bismuth preparation,[1] failed to alter the lesions on his skin and in his mouth. After this, he was given old arsphenamine, 0.4 Gm., every three days for six doses without much improvement. Then he was given four more weekly injections of the bismuth preparation plus an injection of typhoid-paratyphoid vaccine to produce a fever, without benefit.

As all of this treatment had failed, I sent him to Dr. Norman Epstein for intensive therapy, including fever. At this time spirochetes were found in the cutaneous lesions and the Wassermann reaction was positive. Intensive treatment consisted in administering mapharsen, 0.06 Gm., twice daily for eight days and producing two attacks of artificial fever (up to 106 F.) by the hypertherm. Following this, the lesions immediately began to improve and within a month had entirely disappeared. During this time I was giving him the bismuth preparation twice a week. He is still under treatment, presenting no sign of activity. The Wassermann reaction is now 4 plus.

Mrs. J. W. P., a white woman, wife of Mr. J. W. P., was first seen by me when her husband consulted me. Her Wassermann reaction at that time was negative, and she was

1. The preparation used (in doses of 2 cc.) was bismoid (Eli Lilly and Company), which is said to be a stabilized suspension of finely divided bismuth, 25 mg. per cubic centimeter, in a sterile aqueous medium. It has not been accepted by the council on Pharmacy and Chemistry of the American Medical Association.

without evidence of syphilis. However, two months later she showed a faint maculopapular, clinically typical syphiloderm. There were no lesions of the mucous membranes. Her Wassermann reaction had become strongly positive. She was given mapharsen, 0.06 Gm., of the same manufacture as that given to her husband, twice weekly for sixteen injections. The lesions disappeared rapidly within the first two weeks. The Wassermann reaction is still positive.

COMMENT

In this particular instance it seems that some unknown factor in the host rather than in the parasite or the drug determined the course of the disease.

3115 Webster Street.

FIXED DRUG ERUPTION PRODUCED BY DIPHENYLHYDANTOIN SODIUM

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First Assistant in Dermatology and Syphilology,
AND
PAUL A. O'LEARY, M.D.*
ROCHESTER, MINN.

Diphenylhydantoin sodium (phenytoin sodium; dilantin sodium [sodium 5,5-diphenyl-hydantoinate]) has been used extensively both in the United States and abroad in the control

Lesion on arm showing fixed pigmentary eruption.

of chronic convulsive disorders since it was first introduced by Merritt and Putnam in 1937.[1] Most observers are enthusiastic regarding the anticonvulsant merits of the drug, but nearly all emphasize the high incidence of toxic reactions. These may affect the gastrointestinal, the central nervous, the hemopoietic, the cardiovascular or the cutaneous system. Fairly frequently, reactions are noted concurrently in more than one system.

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* From the Section on Dermatology and Syphilology, Mayo Clinic.

1. Merritt, H. H., and Putnam, T. J.: Sodium Diphenyl Hydantoinate in the Treatment of Convulsive Disorders, J. A. M. A. **111**:1068-1073 (Sept. 17) 1938.

A large variety of cutaneous reactions have been attributed to the drug. The incidence of cutaneous signs of toxicity differs widely, from 0 or 1.3 to 35 per cent, although most observers estimate the incidence of cutaneous eruptions to range from 5 to 12 per cent.

The types of cutaneous reactions differ considerably. While erythema morbilliforme and erythema scarlatiniforme predominate, exfoliative dermatitis, urticarial lesions, bullae and ecchymotic, purpuric and petechial eruptions have been reported. Pronounced edema of the face and, recently, hemorrhagic erythema multiforme which terminated fatally have also been recorded in the literature. Gingival hyperplasia, first noted by Kimball,[2] has been observed repeatedly.

An extensive, though not exhaustive, review of the literature failed to reveal any previously recorded instance in which the "fixed" type of drug eruption developed after the ingestion of diphenylhydantoin sodium, and therefore we considered the following case of interest.

REPORT OF A CASE

A white woman, aged 37 years, had suffered from a cerebral vascular accident of the right side of the cortex in 1938. Subsequently, attacks of grand mal developed. These were inadequately controlled until June 1939, when the patient was given 0.1 Gm. of diphenylhydantoin sodium twice daily. For eight weeks she took the drug, with relief from her convulsive disorder and no disturbance of her skin. Thereafter she elected to take the drug only sporadically "when she didn't feel well," and on these occasions she would take 2 capsules (0.2 Gm.) daily for two or three days at a time.

During the summer of 1942 the patient noted the appearance of a "blotchy red rash" on the thighs, arms and trunk. She did not associate the appearance of the eruption with the ingestion of any drug. Eventually the redness subsided, only to recur from time to time in the same locations after the taking of phenytoin sodium. Ultimately pigmentation became prominent and persistent at these sites.

On Jan. 1, 1943, the patient took a single dose (0.1 Gm.) of diphenylhydantoin sodium at noon. By nightfall pronounced swelling and erythema developed on the previously pigmented areas. The swelling and erythema were associated with edema of the left side of her face sufficient to close the left eye. Still she did not relate the drug to the eruption.

The patient was seen in the Section on Dermatology on January 23, at which time the only vestige of her eruption was a small number of nummular pigmented plaques situated on the right thigh, both arms and the trunk. The pigmentation was not uniform in distribution in these plaques but was flecked (fig.).

The patient was given a test amount of diphenylhydantoin sodium in her usual dosage of 0.1 Gm. Forty-five minutes later she returned, displaying acute erythema and edema of the pigmented plaques with a surrounding erythematous halo extending 3 cm. radially. It was suggested that she henceforth omit the use of diphenylhydantoin sodium and endeavor to control the convulsive seizures by substituting phenobarbital, to which she was apparently not sensitive.

2. Kimball, O. P.: Treatment of Epilepsy with Sodium Diphenyl Hydantoinate, J. A. M. A. **112**:1244-1245 (April 1) 1939.

SEVERE TROPICAL ULCER

OSWALDO G. COSTA, M.D., BELLO HORIZONTE, BRAZIL
Assistant in Clinic of Syphilis and Cutaneous Diseases of the Faculty of Medicine, University of Minas Geraes

The following case of tropical ulcer is reported on account of the unusual extent of the ulcer. Various causes have been mentioned as being contributory to the rapid extension of tropical ulcers, including malaria, helminthiasis, trypanosomiasis and undernourishment. My patient had an infection by Ancylostoma duodenale.

REPORT OF A CASE

G. G. S., a Negro boy aged 16, was born in Minas Geraes. He stated that, following the bite of a mosquito on his leg, a small pustule appeared which later ulcerated and spread to the size observed.

Examination showed a round ulcer on the shin and lateral aspects of the lower third of the left leg. It measured 16 by 15 cm. The borders were raised and sharply demarcated and were surrounded by edematous skin. The ulcer consisted of a putrid magma, composed

Tropical ulcer with origin from a mosquito bite.

of necrotic tissue and false membranes and had a peculiar gloss, like that of a mirror. There was a profuse serosanguineous discharge. The patient complained of pain, which was most severe at night, as normally happens in tropical ulcer. There was no enlargement of the femoral glands.

Microscopic examination of the ulcer showed the presence of a fusospirillum. Examination of the stools showed A. duodenale. The Kahn reaction of the blood was negative.

Rua Ceará, 1695.

DERMATITIS VENENATA DUE TO MISTLETOE

LIEUTENANT NORMAN M. O'FARRELL
MEDICAL CORPS, ARMY OF THE UNITED STATES

Among the various plants known to be capable of producing dermatitis, the common mistletoe (Viscum album) has not been incriminated in any previous reports. Because it is widely used for decoration, it must only rarely be a source of dermatitis.

REPORT OF A CASE

Pvt. G. S., of the Eighty-First General Hospital, was one of a detail of men sent out to gather mistletoe for decoration of a dance floor. The next morning he reported at sick call showing on his face and arms streaks of vesicles, which are the indisputable mark of dermatitis due to a plant. In contrast to the usual detective work necessary in such cases, the patient volunteered the information that he was sensitive to mistletoe and that he had had eruptions from this source on previous occasions. Patch tests with leaves and berries of mistletoe produced a vesicular reaction to the leaves in twenty-four hours but no reaction to the berries.

Dr. Laird S. Van Dyck, of New York, established the nonexistence of previous reports of dermatitis from this cause.

Editorials

DERMATOLOGISTS IN THE WAR

It is generally known that the armed forces will need six thousand more physicians by Jan. 1, 1944. This means that an additional number of dermatologists will be required, even though a few of them may not be given satisfactory opportunities to practice their specialty. Every possible attempt will doubtless be made in the future, as has been made in the past, to utilize special knowledge possessed by medical officers.

A later issue of the ARCHIVES OF DERMATOLOGY AND SYPHILOGY will contain a list of dermatologists in active service in the armed forces and in the United States Public Health Service. We can be proud of the large number who have volunteered their services. It appears, however, that the number of older and widely known dermatologists who served in World War I is still somewhat greater than the number of such dermatologists who are in service in the present war. In the last war, for instance, there were seventeen members of the American Dermatological Association, as opposed to ten members in this more extensive conflict. Needless to say, many veterans of World War I later became members of this association.

In regard to the physician between the ages of 38 and 45 who still hesitates to volunteer, an editorial in *The Journal of the American Medical Association* (**122:** 1016 [Aug. 7] 1943) states: ". . . he should realize the added advantage to him of accepting now the commission that is proffered. Should it become necessary in the near future, as seems quite likely, to enlist new activity by the Selective Service Administration and the Officers' Procurement Service to bring in the six thousand physicians that are so certainly required, those recruited by that technic will inevitably begin their service with the minimum commission that is offered, namely that of first lieutenant. Until that technic is installed, the men of special competence and of years beyond those of the recent graduate have the assurance of careful consideration and a commission more nearly in accord with age and experience."

All recognize the splendid record of the members of the medical profession in all former wars. No physician ever had to be drafted. The profession will not fail to do its full duty in the present emergency, and it is confidently expected that the dermatologists will undertake their full share of the responsibility of winning this war.

News and Comment

MEETING OF ASSOCIATION OF MILITARY SURGEONS

What promises to be the most important medical meeting ever held in this nation in time of war will convene in Philadelphia on October 21, when the Association of Military Surgeons of the United States begins its three day session in the Bellevue-Stratford Hotel, the fifty-first meeting of the organization.

The symposium on war medicine will have vital and direct bearing on the health and welfare of the men in the armed forces; it will be of interest to physicians, research specialists and scientists everywhere, as well as to the general public. It is expected that the meeting will be attended by two thousand physicians and surgeons, many of whom have been on active duty in camps and bases throughout the country and on the fighting fronts.

Medicine's methods of meeting the new and complicating factors brought on by mechanized modern warfare will also highlight the sessions. There will be reports and discussions on such new matters as air evacuation, parachute injuries, the physiologic aspects of high altitude flying and dive bombing, tropical medicine, blast injuries, amphibious operations, submarine warfare, immersion and temperature extremes, neurosurgical problems and the whole field of rehabilitation.

At the initial evening session, to be known as "Army night," the President of the United States will deliver his greetings to the convention via radio. There will be addresses by the Chinese Ambassador, Wei Tao-Ming, and by Surgeon General Norman T. Kirk, of the United States Army.

At the following night's session, which will be known as "Navy night," the principal speaker will be the Hon. Frank Knox, Secretary of the Navy. The presiding officer will be Rear Admiral Ross T. McIntyre, Surgeon General of the United States Navy and personal physician to the President.

Nationwide hook-ups will carry reports of the meeting to the public at large and by short wave broadcast to the people in the Allied Countries, who will be apprised of the progress of the convention and its meaning to the men in arms and to national health in general.

The convention, with its score of exhibits and meetings, will occupy all available floor space in the Bellevue-Stratford Hotel. The program will list, besides general sessions, a series of forum lectures and teaching panels, as well as a great number of film presentations.

Correspondence

DERMATITIS DUE TO NAIL POLISH FOUNDATION

To the Editor:—I am particularly interested in the article published by Lieutenant Joseph M. Shelton (MC), U. S. N. R. (ARCH. DERMAT. & SYPH. **48**:197 [Aug.] 1943).

For several years I have been trying to obtain from many manufacturers of nail polish a preparation which does not contain nitrocellulose.

Practically all patients with nail polish dermatitis that have come under my observation in the past five years when tested with the raw ingredients of nail polish have shown positive reactions to a solution of nitrocellulose. It seemed impossible to obtain a polish from which the nitrocellulose was eliminated that would remain on the nails without peeling, owing to the lack of a plasticizer.

In June 1940 I took my problem to the Vorac Corporation, of Newark, N. J., manufacturers of plasticizers and nail polishes. With the collaboration of the president, Mr. Anderson, I attempted to find the real sensitizer in the nail polish.

The dry nitrocellulose was washed and filtered three times and allowed to dry. Patch tests were made on 5 persons known to be allergic to the dry product. The reactions, which had previously been positive to the nitrocellulose solution, were now reversed. We decided that something else must be the irritant and tested these patients with a synthetic resin used as a plasticizer. All of them showed positive reactions to the synthetic resin. A polish was then made which contained nitrocellulose and a substitute resin. Two patients tested with this resin showed negative reactions. It is interesting to note that 1 of these patients was able to use the finished product without any further nail polish dermatitis, in spite of the fact that it contained nitrocellulose. The other patient showed a reaction which proved to be due to the pigment used in the preparation.

In view of the foregoing results, it is my opinion that in most cases of nail polish dermatitis it is the solvent rather than the nitrocellulose that is the sensitizer and that a polish can be made up with nitrocellulose provided a proper synthetic resin can be obtained.

In view of the large number of cases of nail polish dermatitis that confront dermatologists today, I feel that these observations are of particular interest.

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Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

TREATMENT OF LEG ULCERS WITH BLOOD AND CONCENTRATED PLASMA. MEYER NAIDE, Am. J. M. Sc. **205**:489 (April) 1943.

Naide treated 15 patients with ulcer of the leg by means of local applications of whole blood or plasma. Nine of the 10 patients with ischemic ulcers had extensive grades of arterial occlusive disease; 5 of these ulcers healed and 1 was still improving at the time of the report. Four of the 5 varicose ulcers were healed and the fifth nearly so. All of the patients had previously been treated by various methods, without improvement.

Treatment consisted of repeated applications of blood or solution of dried plasma so that the material formed a firm coating over the ulcer. Inflammatory reaction and pain were relieved rapidly. One ulcer broke down after remaining healed for four months.

STUDIES ON THE PENETRATION OF SULFONAMIDES INTO THE SKIN: I. PENETRATION OF SULFONAMIDES FROM VARIOUS OINTMENT BASES INTO THE INTACT SKIN OF GUINEA PIGS; AND A NEW METHOD OF ANALYSIS OF TISSUE SULFONAMIDES. ERNEST A. STRAKOSCH and WILLIAM G. CLARK, Am. J. M. Sc. **205**:518 (April) 1943.

Strakosch and Clark report the results of chemical analysis of sulfanilamide in the tissues of guinea pigs after the application of the drug to the intact skin in four typical water in oil and three oil in water emulsion ointment bases and in several concentrations. There was no correlation between the penetration of the drug and the type of ointment base, but there was greater penetration from a base consisting of oleic acid, white petrolatum, oleic acid ester and amide of diethanolamine ("hydrosorb") than from the other bases. Increasing the concentration of sulfanilamide from 1 per cent to 10 per cent resulted in penetration of only slightly greater amounts of the drug.

PINTA: A REVIEW OF RECENT ETIOLOGIC AND CLINICAL STUDIES. HERMAN BEERMAN, Am. J. M. Sc. **205**:611 (April) 1943.

Beerman discusses pinta because of the numerous military personnel in the tropics and the expectation that examples of this disease will be observed in this country after the war. It is estimated that 1,000,000 persons in Latin America are affected by pinta, and it is endemic in certain large areas. The development of modern knowledge of the disease dates to the identification of the causative spirochete in 1938. The exact position of the disease is not clear. Hudson regards it as one with syphilis, yaws and bejel, while many others think the relationship may have been closer in the remote past than is now the case. At least one investigator found that syphilis does not render a patient immune to pinta, and in the latter disease it is possible to produce experimental reinfection.

Eosinophilia is said to occur in 75 per cent of the cases of pinta, and local eosinophilia also occurs in the cutaneous lesion and in the enlarged lymph nodes. Various observers have reported positive complement-fixation and flocculation reactions in from 60 to 100 per cent of the cases at different stages of the disease. The serologic reactions are usually not influenced by treatment which is similar to that given for syphilis and yaws.

There is evidence that an insect vector may be concerned in the transmission of pinta. Though the spinal fluid has received considerable attention, there is conflict in the various reports as to the nature and frequency of the changes. Cardiovascular involvement is relatively common.

Beerman's review is concise, clear and well supplied with references.

LYNCH, St. Paul.

CHEMOTHERAPEUTIC PROPHYLAXIS WITH SULFONAMIDE DRUGS. F. W. REYNOLDS, M. S. EVANS and F. B. WALSH, Am. J. Syph., Gonor. & Ven. Dis. **27**:2 (Jan.) 1943.

Sulfathiazole and sulfadiazine when administered in doses comparable to those used in the chemotherapeutic prophylaxis of gonorrhea (4 Gm. in twenty-four hours) produce definite untoward transitory effects on visual efficiency. These drugs should not be used indiscriminately, especially for persons who constantly require maximum visual efficiency, whether in the armed forces or in civilian life.

REINFECTION IN SYPHILIS. A. G. SCHOCH and L. J. ALEXANDER, Am. J. Syph., Gonor. & Ven. Dis. **27**:16 (Jan.) 1943.

Data are presented to show that reinfection in syphilis is not rare and that it occurs more commonly with intensive arsenotherapy for early syphilis than with orthodox treatment schedules. Ten cases of reinfection are recorded. Four patients sustained reinfections following orthodox antisyphilitic therapy. Six patients of 103 sustained reinfections after ten day intensive arsenotherapy for early syphilis (1,200 mg. mapharsen). Dark field examination and quantitative reagin titer curves were used to support clinical observations. Objective data on infectiousness of contents responsible for reinfection are recorded. All patients were observed by the authors for both infections.

FURTHER EVIDENCE CONCERNING THE SPECIFICITY OF THE LYMPHOGRANULOMA VENEREUM COMPLEMENT-FIXATION TEST IN SYPHILIS. A. W. GRACE, M. F. SHAFFER and G. RAKE, Am. J. Syph., Gonor. & Ven. Dis. **27**:44 (Jan.) 1943.

Serums from persons with congenital syphilis who give negative Frei reactions do not fix complement in the presence of antigen from the virus of lymphogranuloma venereum. In contrast, there is a high frequency of positive reactions obtained with serums from persons with venereally acquired syphilis. These observations further strengthen the belief that during venereal exposure resulting in syphilis or other sexually transmitted infection a concomitant and often latent infection with the agent of lymphogranuloma venereum frequently occurs.

EVALUATION OF YOLK SAC ANTIGEN FOR FREI TEST. H. O. CURTH, Am. J. Syph., Gonor. & Ven. Dis. **27**:47 (Jan.) 1943.

An antigen prepared from the yolk sacs of chick embryos inoculated with the virus of lymphogranuloma venereum gave correct results in about 85 per cent of cases when compared with results obtained from a reliable Frei antigen from human pus. In 11 cases, however, the reaction to the antigen was accompanied by a positive reaction to the control material, making the result of the test equivocal and reducing the definite agreement to 78 per cent. A high percentage of apparently nonspecific reactions was encountered. While the yolk sac antigen is apparently the most reliable preparation for the Frei test available commercially, the reliability of a positive reaction to this antigen must still be seriously questioned.

THE MICROSCOPIC PATHOLOGIC APPEARANCE OF THE AORTA IN TREATED AND UNTREATED CASES OF SYPHILITIC AORTITIS. E. G. HOWE, Am. J. Syph., Gonor. & Ven. Dis. **27**:50 (Jan.) 1943.

It would appear from the present study of syphilitic aortas that the amount of cellular infiltration into the aortic wall bears an inverse relationship to the amount of arsenical therapy received. Patients who had received twelve or more injections of an arsenical showed much less cellular infiltration than untreated patients or than patients who had received forty or more injections of a heavy metal with less than ten injections of an arsenical.

The amount of cellular infiltration showed no correlation with the duration of the infection with syphilis and little correlation with the intensity or the duration of treatment with bismuth or mercury.

REUTER, Milwaukee.

ANTHRAX. HERMAN GOLD, Arch. Int. Med. **70**:785 (Nov.) 1942.

Gold reviews his experience in the treatment of 60 cases of anthrax. He states that the diagnosis should always be confirmed bacteriologically, even though accurate clinical diagnosis may be easy. Incision, excision and local injection of chemicals or serum are strongly deprecated. He used antianthrax serum in 21 cases with only 1 death. Adequate dosage is essential, with treatment given every twelve to twenty-four hours until edema is checked; adenopathy may persist for days or weeks but gradually disappears without any therapy. In 2 of the patients treated with serum urticaria and angioneurotic edema developed, and 1 had a "nitritoid" type of reaction.

Sulfonamide compounds were used in treatment of 42 patients, with excellent results in 39, the average period of disability being reduced to 40 per cent of that observed when treatment was with serum alone. Sulfapyridine was more effective than other drugs in the group, but the greater efficiency was partly overcome by the greater incidence of reactions; hence sulfathiazole was considered the drug of choice. If the edema was not controlled by the third day of chemotherapy, Gold then gave large doses of antianthrax serum.

POLYMYOSITIS. DOUGLAS GOLDMAN, Arch. Int. Med. **70**:822 (Nov.) 1942.

Goldman reports a fatal case of widespread inflammatory lesions of the skeletal muscles, associated with early cutaneous lesions which led him to place the disease in the dermatomyositis group in spite of the relatively normal appearance of the skin in the late stages of the disease. The nature of the eruption was such that correct diagnosis was possible only in retrospect. The neurologic clinical manifestations served only to confuse the issue.

URINARY SEDIMENT IN VISCERAL ANGIITIS (PERIARTHRITIS NODOSA, LUPUS ERYTHEMATOSUS, LIBMAN-SACKS "DISEASE"). MARCUS A. KRUPP, Arch. Int. Med. **71**:54 (Jan.) 1943.

Krupp studied the urinary sediment in 21 cases of periarteritis nodosa, lupus erythematosus and Libman-Sacks "disease." In 7 cases no specific changes were discovered but in 14 there were red blood cells, red cell casts, oval fat bodies, fatty casts, broad casts and abnormal quantities of protein in the same specimen of urine. He states that this sediment is unusual and does not occur with glomerulonephritis or other common renal lesions.

SICKLE CELL ANEMIA IN THE WHITE RACE. M. A. OGDEN, Arch. Int. Med. **71**:164 (Feb.) 1943.

Dermatologists have an interest in sickle cell anemia because of the frequency with which ulcers are observed on the legs of patients. Ogden reports 2 cases of sickle cell anemia (without ulcers) and states that presence of the sickling trait in a white person is a definite proof of admixture of Negro blood in the immediate or remote ancestry.

EFFECTS OF VITAMIN A DEPLETION IN YOUNG ADULTS. SADIE BRENNER and LYDIA J. ROBERTS, Arch. Int. Med. **71**:474 (April) 1943.

As part of a general study of vitamin A deficiency Brenner and Roberts report the results of biopsies made at intervals of four and seven months. They state that there were no measurable differences in the subcutaneous structure of the hair follicles and of the sweat and sebaceous glands from that found prior to the experimental diet. Visibility of the capillaries remained good, demonstrating that there was no keratinization of the epithelial tissue.

THE BLOOD CHOLESTEROL. SIDNEY WEINHOUSE, Arch. Path. **35**:438 (March) 1943.

Studies on cholesterol are of interest to dermatologists because of the various dermatoses which are reputed to be associated with cholesterol metabolism. Weinhouse points out that though a great deal of information has accumulated as a result of clinical and experimental studies, many conclusions have rested on mistaken or confused ideas as to the normal levels and the metabolism of cholesterol. This subject is discussed in a 55 page review.

Many studies have reported the normal concentration of cholesterol as lying between 110 and 260 mg. per hundred cubic centimeters of serum or plasma, but recent studies have established high normal average values and a wide range of normal variation. Values as high as 376 and 392 mg. have been regarded as normal by two groups of investigators. The cholesterol level of the blood is low at birth and increases gradually throughout childhood. Advanced age probably does not influence the cholesterol level. When differences in body build are not associated with endocrine disease, pyknic and asthenic women show only slight differences while pyknic men have higher serum lipid levels than do asthenic men. Certainly in animals and probably in human beings the cholesterol level is increased during emotional excitation. The level is also increased after muscular effort. There are also variations in blood levels during menstruation and pregnancy.

There is considerable doubt whether the character and quantity of food has any influence on the level of cholesterol in the blood, but when cholesterol is mixed with lecithin it produces appreciable rises in the level, probably through finer emulsification and more efficient absorption.

In addition to discussing the normal metabolism of cholesterol, Weinhouse reviews the abnormal states associated with hepatic, renal or thyroid disease, atherosclerosis, diabetes and xanthomatosis. While it is well known that relatively great changes in the cholesterol level are observed in hypothyroidism, he points out that in hyperthyroidism determinations of the cholesterol content of the blood probably have little clinical usefulness.

Reading this excellent review must lead any dermatologist to the conclusion that there is need for critical review of the observations and conclusions reported in many studies of the association between various dermatoses and disturbed metabolism of cholesterol.

LYNCH, St. Paul.

LEPROSY: THE CORRELATION OF ITS CLINICAL, PATHOLOGIC, IMMUNOLOGIC AND BACTERIOLOGIC ASPECTS. V. PARDO-CASTELLO and FRANCISCO R. TIANT, J. A. M. A. **121**:1264 (April 17) 1943.

Pardo-Castello and Tiant propose a new classification of the clinical forms of leprosy which would correlate the pathology, immunology and bacteriology of the disease. The old conception of "cutaneous," "neural" and "mixed" types of leprosy is not helpful, since the great majority of patients with leprosy present symptoms and signs of cutaneous, neural and visceral involvement. Therefore, most cases of leprosy would fall under the heading of "mixed" leprosy.

In leprosy the pathologic changes may be grouped in three categories: lepromatous, tuberculoid and simple inflammatory, which the authors call nonspecific. To the trained eyes these pathologic changes have clinical equivalents: the lepromatous, represented by the nodular infiltrative lesions; the tuberculoid, represented by flat, infiltrated, annular or ringlike, small nodular lesions, and the nonspecific, represented by the macular manifestations of the skin and the simple dystrophic neural manifestations.

Lepromatous lesions are extremely rich in leprosy bacilli, while the tuberculoid and nonspecific lesions are paucibacillary. The immunologic lepromin tests are negative in lepromatous and positive in tuberculoid types. The nonspecific changes represent transitional stages, the changes may remain nonspecific for a long time, or the disease may develop into the lepromatous or the tuberculoid form.

When a drop of a 1:1,000 solution of a histamine salt is placed on a normal skin and a needle prick is made through the liquid, a small wheal surrounded by an erythematous halo develops. When the sensitive nerve endings are paralyzed or destroyed, the phenomenon occurs as far as whealing, but no erythematous halo develops around the wheal. The normal response to histamine is called the positive reaction; the absence of erythematous reaction around the wheal characterizes the negative reaction. Therefore, in the cutaneous lesions of leprosy the result of the histamine test is always negative.

The lepromin test consists essentially in the intradermal injection of an antigen prepared from lepromatous tissues rich in leprosy bacilli. In Cuba all attempts to consider the test of any value in diagnosis have been abandoned. Cuba is a leprous country, and all healthy men and women react positively to lepromin because they have been in contact with leprous persons for many years and have developed immunity to leprosy. The lepromin test is helpful in the classification of cases of leprosy, and it has prognostic value. Lepers with a negative reaction to lepromin have the lepromatous type of leprosy, which has a very poor prognosis.

HENSCHEL, Denver.

THE ALLERGENIC PROPERTIES OF THE VEGETABLE GUMS: A CASE OF ASTHMA DUE TO TRAGACANTH. H. HAROLD GELFAND, J. Allergy **14**:203 (March) 1943.

Published reports of sensitivity to vegetable gums indicate that the chief sources of sensitization are karaya gum in hair-waving lotions and acacia (gum arabic) in the offset sprays used by printers. Other persons exposed to occupational contact with the gums include confectioners, employees of gum plants, persons engaged in the manufacture of cigars, metal polish, matches, porcelain and pottery and others. A list of the known sources of possible contact with the allergic gums is presented.

The usual mode of contact is by inhalation, but ingestion, injection and surface contact have also accounted for reactions. The morbid processes include vasomotor rhinitis, bronchial asthma, urticaria, atopic dermatitis, angioneurotic edema and gastrointestinal disturbances.

Gelfand reports the case of a 26 year old white woman with asthma due to tragacanth. The patient was found, by both direct and passive transfer tests, to be sensitive to tragacanth and acacia but not to karaya.

Acacia (from Acacia senegal) and tragacanth (from Astragalus gummifer) are obtained from plants which, although differing in genus and species, are members of the same family (Leguminosae). Karaya, on the other hand, belongs to an entirely different family (Sterculiaceae). This fact may have a bearing on the antigenic relationship of the gums.

INSULIN HYPERSENSITIVITY WITH DESENSITIZATION: REPORT OF A CASE. MYRON A. WEITZ, J. Allergy **14**:220 (March) 1943.

Reactions to insulin are usually of an allergic nature. The reaction may be due to hypersensitivity to the insulin factor itself, to the pancreatic tissue of the specific animal source or to some extraneous substance of the pancreas not removed in the manufacture of the product or, since the advent of protamine zinc insulin, to hypersensitivity to these added substances.

The symptoms of insulin allergy are of three types: (1) mild reactions at the site of injection, (2) severe reactions at the site of injection and (3) generalized reactions. In the last group there is a general or systemic reaction manifested by cutaneous, circulatory and gastrointestinal symptoms. Urticaria and edema are common and are frequently preceded by numbness, tingling and intense itching of the involved parts. Swelling of the mucous membrane of the mouth and larynx may occur, causing respiratory embarrassment. Nausea, vomiting and abdominal cramps are not infrequent accompaniments. Circulatory collapse and general prostration may take place.

The author reports a case of generalized urticaria in a 60 year old white woman. Attacks were produced by both protamine zinc insulin and regular beef insulin.

Intradermal tests to beef and pork protein gave negative reactions. Intradermal and passive transfer tests to protamine zinc insulin, beef insulin and crystalline insulin gave positive reactions.

Desensitization with crystalline insulin was successful on the fifth day. The dosage varied from 0.1 unit a few times a day to 10 units twice daily. Evidence of desensitization was based on cessation of symptoms with continued use of various types of insulin and negative reactions to direct and passive transfer tests with different insulins.

MENDELSOHN, New York.

CONTRIBUTION TO THE TREATMENT OF ESSENTIAL PRURITUS AND KRAUROSIS VULVAE. E. KLAFTEN, J. Clin. Endocrinol. **3**:218 (April) 1943.

Without denying the role played by other factors, Klaften emphasizes the importance of ovarian failure in the pathogenesis of pruritus vulvae, kraurosis vulvae and leukoplakic vulvitis. He outlines a scheme of treatment employing local use of an estrogen-containing ointment and parenteral administration of estradiol benzoate. Of 54 patients with pruritus, 74 per cent were cured or greatly improved. Slightly less satisfactory results were observed in the other diseases.

EFFECT OF ESTRADIOL AND DIETHYLSTILBESTROL UPON THE ATROPHIC HUMAN BUCCAL MUCOSA, WITH A PRELIMINARY REPORT ON THE USE OF ESTROGEN IN THE MANAGEMENT OF SENILE GINGIVITIS. M. J. RICHMAN and A. R. ABARBANEL, J. Clin. Endocrinol. **3**:224 (April) 1943.

Like a few other observers, Richman and Abarbanel had noted a dryness or burning sensation of the mouth in many women in the climacteric. Their report is based on 25 women studied as to gross oral manifestations, subjective symptoms and histologic structure of the buccal mucosa. Within six months after surgical castration the oral mucosa tended to show pallor, a grayish pink color, an anemic appearance and beginning atrophy of the prickle cell layer. After two years or more diffuse or patchy white or gray areas, a tendency to bleed easily, atrophy and areas of leukoplakia were observed; symptoms were complained of more frequently by patients in this group. After estrogenic therapy there was improvement of the symptoms and of all the signs except in the leukoplakic areas.

FURUNCULOSIS: ETIOLOGY AND TREATMENT. BRODA BARNES, J. Clin. Endocrinol. **3**:243 (April) 1943.

Barnes studied the cases of 16 college students with furunculosis and found no correlation between the values for hemoglobin and the development of boils. There was no evidence of malnutrition, but all of the patients had subnormal temperatures, 97.0 to 97.6 F. Of 14 patients whose basal metabolic rate was determined, 10 had rates of —10 per cent or lower and only 1 had a rate above ±0 per cent. Thyroid therapy was started for 14 patients, and in none did further boils develop.

MORPHOLOGICAL STRUCTURE OF RICKETTSIAE. HARRY PLOTZ, JOSEPH E. SMADEL, THOMAS F. ANDERSON and LESLIE A. CHAMBERS, J. Exper. Med. **77**:355 (April) 1943.

Plotz and his associates discuss the structure of rickettsias as seen in Rocky Mountain spotted fever and other fevers. The details are well demonstrated in high power photomicrographs.

LYNCH, St. Paul.

SKIN DISTURBANCES IN DIABETES MELLITUS: THEIR RELATION TO VITAMIN DEFICIENCIES. A. RUDY and R. HOFFMANN, New England J. Med. **227**:893 (Dec. 10) 1942.

Rudy and Hoffmann state that the cutaneous manifestations in diabetes mellitus are frequently of the pellagrous type and that signs of deficiency of one or more components of

the vitamin B complex often can be revealed. They are not related to the glycosuria or hyperglycemia but depend on an increased vulnerability of the skin resulting from the vitamin deficiency.

Cases are reported of cutaneous lesions under the breasts, about the anus and on the hands, feet and ears. They had the clinical appearance of monilia infections and cleared up after the administration of vitamin B complex, particularly of nicotinic acid, without local treatment.

Patients with the more stubborn lesions require fairly large doses parenterally as well as orally. Recurrences are not uncommon, and the administration of vitamin B complex may have to be continued indefinitely.

RONCHESE, Providence, R. I.

DERMATITIS DUE TO TYROGLYPHUS LONGIOR, GERV., VAR. CASTELLANII, HIRST, IN CHEESE DUST. E. W. PROSSER THOMAS, Brit. J. Dermat. **54**:313 (Dec.) 1942.

Thomas reports a diffuse erythematous dermatitis of the forehead, face, ears and neck, with slight edema of the eyelids and involvement of the flexor surfaces of the forearm, in a railway loader. The eruption was due to cheese dust in which the mite Tyroglyphus longior, Gerv. was found. The cheeses mainly attacked are those that have been left a considerable time in store. The mites, which are said to be present in most dairies and can be found in dust and scrapings from the shelves, apparently crawl on to the cheese, select a minute hole or crevice and eat their way in; eggs are laid and a flourishing colony is soon established. On the surface of the cheese a coating of fine powder forms, which may be a quarter of an inch (0.6 cm.) thick, composed of layer on layer of dead bodies of mites, macerated skins, feces, minute particles of uneaten cheese and the living mites themselves. Mite-infected cheese can be recognized by this fine brown powder and by the numerous small holes and cavities.

DERMATITIS FROM EXPOSURE TO TEAR GAS. JOHN T. INGRAM, Brit. J. Dermat. **54**:319 (Dec.) 1942.

Ingram reports a case of dermatitis in an officer exposed to a fairly high concentration of tear gas (chloroacetophenone) in a confined space for three quarters of an hour. About seven hours later he noticed irritation of the skin,. especially in the flexures, quickly followed by a morbilliform eruption which soon became blistered. Under simple treatment with baths and calamine lotion the condition resolved in two weeks and left the patient with no ill effects.

CUTANEOUS AND SUBCUTANEOUS NODULES WITH JUXTA-ARTICULAR INFILTRATIONS AND RHEUMATOID SYMPTOMS. F. PARKES WEBER, Brit. J. Dermat. **55**:1 (Jan.) 1943.

Parkes Weber reports 2 cases which were clinically characterized by severe rheumatoid symptoms and especially by cutaneous and subcutaneous nodules and juxta-articular thickenings of tendon sheaths and other fibrous structures. In 1 case there was almost certain connection with lipid infiltration.

DERMATITIS VENENATA CAUSED BY SMOKE. J. V. LANDOR, Brit. J. Dermat. **55**:17 (Jan.) 1943.

Landor reports severe dermatitis occurring on the exposed parts in 13 persons who were exposed to the smoke of firewood from the "binjai" tree. The lesions were chiefly vesicles containing serous fluid on an erythematous base. The binjai tree is commonly known as the wild mango. All of the patients improved fairly quickly when the use of binjai firewood was discontinued and were aided by the use of simple lotions, such as a 6 per cent solution of coal tar in water.

BLUEFARB, Chicago.

PYODERMA ULCEROSUM TROPICALUM. O. ALPINS, M. J. Australia **1**:30 (Jan. 9) 1943.

By the term "pyoderma ulcerosum tropicalum" is described an infectious cutaneous disease which has affected a great number of men serving in the northern part of Australia. The author has seen about 300 persons with the disease.

The eruption starts mainly on exposed parts around the hair follicles. In most cases the infection follows injury. The incubation period is short, varying from six to twelve hours. The lesion commences with one or more discrete vesicles. Eventually a deep ulcer develops.

The disease is produced by a virulent hemolytic strain of Streptococcus contaminated by a secondary staphylococcic infection.

The author differentiates pyoderma ulcerosum tropicalum from septic sores ("Barcoo Rot"), which begin with a vesicle which on bursting leaves a superficial ulcer with thickened margins. He thinks septic sores are mostly of diphtheritic origin. He also differentiates pyoderma

ulcerosum tropicalum from tropical ulcer (tropical phagedena), which is characterized by the presence of a chronic sore, covered with a false membrane of purulent and necrotic tissue which on being cleaned away leaves a raw base surrounded by indurated edges. Schaudinn's spirochete is believed to be the cause. Alpins distinguishes pyoderma ulcerosum tropicalum from tropical ecthyma of Castellani, which is a nodular lesion which breaks down and forms an ulcer with undermined edges. It is due to Staphylococcus tropicalis.

Ointments containing sulfonamide compounds, especially sulfapyridine, are curative for pyoderma ulcerosum tropicalum.

HENSCHEL, Denver.

Society Transactions

MANHATTAN DERMATOLOGIC SOCIETY

FRED WISE, M.D., *President*

ANTHONY C. CIPOLLARO, M.D., *Secretary*

Oct. 13, 1942

Mycosis Fungoides of the Chest with Parapsoriasis en Plaques of the Body. Presented by DR. E. WILLIAM ABRAMOWITZ.

Mr. H. S., aged 53, from the New York Skin and Cancer Hospital, was born in England. His past history is irrelevant except that he had typhoid when he was 24 years old. Following that he noticed an eruption on the right side of his chest. About the same time he noticed many half-dollar–sized lesions on his body.

He was first seen in November 1927. He then presented a sharply limited erythematous crusted dermatitis which covered the right mammary area. This patch had been present for fourteen years. He also presented medallion-shaped and oval brownish and slightly scaly patches on his trunk and extremities. He received several roentgen treatments to the right side of his chest, with partial improvement of the eruption in this area. He returned in April 1929 when he received roentgen treatment again to the lesion on the chest and ultraviolet radiation to the lesions on the trunk.

He returned in July 1942. In the meantime he had received treatment from a general practitioner for chronic prostatitis. In the past year he has been complaining of flushes and headaches.

The patches on the sides of the trunk are about the same as they were in 1929. They become red in warm weather or on being rubbed. The lesion on the right side of his chest is infiltrated, scaly and red. A gland in the right axilla is palpable. Numerous seborrheic keratoses are present on his chest and back. The lesion on the right mammary area responded to roentgen treatment and injections of sodium arsenate. The right axillary gland also receded. The Wassermann reaction of the blood was negative. The blood count shows a mild leukopenia but no other abnormalities.

A specimen for biopsy from the eczematous lesion on the right side of the chest in 1927 was reported as showing parapsoriasis with secondary eczematization. A specimen from one of the lesions on the trunk was reported as characteristic of parapsoriasis. A recent specimen from the patch on the right mammary area, however, was reported as typical of mycosis fungoides. Reexamination of the old slide made in 1927 indicated that it was suggestive of mycosis fungoides.

DISCUSSION

DR. HERMAN SHARLIT: There is nothing to add; we must accept the diagnosis.

DR. DAVID BLOOM: The existence of mycosis fungoides for twenty years without extension seems to me extremely unusual. At present the clinical appearance is not that of mycosis fungoides.

DR. ISADORE ROSEN: It would be unusual for a patient having the en plaques type of parapsoriasis, proved microscopically fifteen years ago, to acquire at the present time one lesion of mycosis fungoides without changes taking place in any of the other lesions. I suggest that instead of mycosis fungoides this is some form of chronic dermatitis similar to that seen in matchbox dermatitis.

DR. WILBERT SACHS: In 1928 or 1929, two pieces of tissue were taken; one was diagnosed parapsoriasis and the other piece eczema. From such slides, one cannot at this time make a diagnosis of mycosis fungoides. However, a recent biopsy shows a definite picture of mycosis fungoides. I believe that a patient with parapsoriasis can remain with parapsoriasis throughout and still acquire mycosis fungoides independent of the parapsoriasis. I do not believe that the lesion on the breast has anything to do with the lesion on the side of the chest. I think the patient has two separate and distinct diseases: One is the original parapsoriasis, and now in addition to that the patient has mycosis fungoides. Histologically, I cannot say that the original slide, made in 1928, showed mycosis fungoides.

DR. E. WILLIAM ABRAMOWITZ: Although parapsoriasis was the diagnosis of the eruption on the trunk, I suspected the lesion on the chest to be mycosis fungoides. This has now been confirmed after fifteen years. I do not recall another case in which there were reported definite lesions of parapsoriasis en plaques together with mycosis fungoides in the same patient at the same time.

Mycosis Fungoides. Presented by DR. ANTHONY C. CIPOLLARO.

L. S., aged 63, first came to the New York Skin and Cancer Hospital on Dec. 30, 1941, and at that time he had an ulcerated lesion at the base of the left thumb of three months' duration. The lesion was about 4 cm. in diameter and was elevated about 1 cm. above the surface of the skin. There were no other ulcers. The palms were dry, scaly and erythematous. There were slightly elevated scaly patches on the lateral surface of the right leg, which suggested the possibility of parapsoriasis. A piece of tissue was removed from the edge of the ulcer, and the histologic report was "possible mycosis fungoides." He received one medium voltage (135 kilovolts), slightly filtered (3 mm. of aluminum) roentgen treatment, consisting of one erythema dose (550 r). This lesion completely disappeared in about three weeks and has never recurred.

On Feb. 4, 1942 scaly, erythematous and infiltrated patches developed on various parts of the body, especially on the hands, forearms, feet and legs. A diagnosis of mycosis fungoides was made, and these lesions promptly disappeared with fractional unfiltered roentgen irradiation (75 r weekly). Since that date he has had exacerbations and remissions of his eruption, not only with plaque formation but with development of ulcerated lesions, especially about the toes and fingers. As soon as old lesions disappear under the influence of roentgen therapy, new lesions appear. He is much worse now than he was ten months ago.

The patient has had a complete physical examination in the medical department of the New York Post-Graduate Medical School and Hospital. The results were essentially normal. There was no evidence of visceral involvement. Several blood counts were made. Bone marrow obtained by sternal puncture showed: polymorphonuclear leukocytes, 38 per cent; lymphocytes, 27 per cent; blastocytes, 1 per cent; metamyelocytes, 5 per cent; monocytes, 3 per cent; myelocytes, 4 per cent, and nuclear red blood cells, 22 per cent. The blood count showed: red cells, 4,080,000; white cells, 7,100; hemoglobin content, 89 per cent; polymorphonuclear leukocytes, 71 per cent; monocytes, 4 per cent; lymphocytes, 22 per cent, and band forms, 3 per cent. Tests of the urine and blood for sugar gave normal results. The Wassermann and Kahn reactions of the blood were negative.

The patient is under continual treatment with roentgen rays.

DISCUSSION

DR. ISADORE ROSEN: I had an opportunity to see this man on his first visit to the clinic. At that time he presented a single dollar-sized raised infiltrated lesion with central ulceration, strongly suggestive of leukaemia cutis. On examining his body we found on the lower extremities large brownish red slightly scaly nonpruriginous lesions which suggested the en plaques type of parapsoriasis. After roentgen treatment the lesion on the hand rapidly regressed. Tonight there is no question as to the diagnosis. He presents lesions which are typical of one of the lymphoblastomas, probably mycosis fungoides.

DR. WILBERT SACHS: In the original lesion it was not easy to make a differential diagnosis as to the type of lymphoblastoma. The cells develop so fast that one cannot always say whether the disease is a mycosis fungoides, Hodgkin's disease or leukemia. All one can do is to call it lymphoblastoma. Of course, the second lesion was more definitely mycosis fungoides.

DR. E. WILLIAM ABRAMOWITZ: I have seen patients whose diseases have been called monocytic leukemia, aleukemia, leukemia and lymphatic or myelogenous leukemia. Autopsy also revealed a difference of opinion as to the type of lymphoblastoma.

DR. DAVID BLOOM: As this is a typical eruption of mycosis fungoides, the appearance of the tumor on the finger as a first manifestation makes this mycosis fungoides à tumeur d'emblée.

DR. FRED WISE: With reference to the remarks made by Dr. Abramowitz, I had occasion to discuss the question of interpretation of sections from lesions of mycosis fungoides with the elder Jadassohn. He stated his belief that the difficulties concerning some sections for diagnosis could be overcome by use of a number of different staining technics instead of one or two methods.

DR. ANTHONY C. CIPOLLARO: The lymphoblastomas respond extremely well to roentgen rays of various wavelengths. In most cases roentgen rays produced with 50 kilovolts are as efficacious as those of higher voltages and added filtration. In this particular patient some of the ulcerated lesions responded to low voltage unfiltered rays while others responded

equally well to filtered high voltage radiation. I have not paid much attention to the scaly patches. So many ulcers developed that it was necessary for the patient to be treated several times weekly.

Dermatomyositis Improved by the Oral Administration of Dihydrotachysterol. Presented by DR. MAURICE J. COSTELLO.

Mrs. H. N., a Russian Jewess aged 56, was presented before this society on March 12, 1940, as having scleroderma due possibly to adrenal neoplasm. A detailed account of her history and the results of physical examination and laboratory findings will be found in the ARCHIVES OF DERMATOLOGY AND SYPHILOGY (**42**:969 [Nov.] 1940). The patient at that time presented a severe degree of dermatomyositis, accompanied by pain and stiffness on motion due to the hidebound condition of the skin, profound fatigue, loss of weight and loss of strength.

She has received many forms of therapy, including administration of a proprietary preparation of pancreas (padutin), desoxycorticosterone acetate and nicotinic acid, local therapy with ointments containing vitamins A and D and ultraviolet radiation, but improvement began at the time when dihydrotachysterol was administered by mouth in doses of 20 drops of a 0.5 per cent solution in oil twice a day.

Improvement is indicated by (1) a gain of more than 30 pounds (13.5 Kg.) in weight, (2) decrease in the degree of sclerodermatous infiltrated areas, permitting greater mobility of all the joints, and (3) a return to normal of strength and feeling of well-being.

DISCUSSION

DR. E. WILLIAM ABRAMOWITZ: The internists believe that scleroderma is associated with visceral disorders. They cite cases in which there was improvement with use of deinsulinized pancreatic extract (depropronex) and also with local applications of mecholyl by iontophoresis or wet dressings. Physicians engaged in the practice of dermatology before any of these methods were used saw patients get well with baking and massage and no medication. I think there should be more interest in the systemic aspect of these patients than there has been hitherto. It may help to a clarification of the various types of scleroderma.

DR. GEORGE LEWIS: There is no doubt that this patient is a great deal better than when last presented. Whether the improvement is due to the present therapy is open to some doubt because of the possibility of spontaneous involution, which occasionally occurs in scleroderma.

DR. WILBERT SACHS: Is it to be assumed that the drug caused improvement of the scleroderma or of the dermatomyositis? I should like to know if a biopsy was made to prove either one of those diagnoses. There is no question that the patient had a severe disease. I should like to point out that a sclerodermatous change is entirely different from the disease scleroderma.

DR. HOWARD FOX: It may be a coincidence that this patient has gained 30 pounds (13.5 Kg.) in weight and that her hand and fingers are much less hidebound and stiff than before dihydrotachysterol was used. It seems reasonable, however, to give the credit to the drug. It has been unusual in my experience to see the progressive type of scleroderma undergo involution. The process is arrested in many cases, but the skin does not return to normal. Even in localized scleroderma the involution which may occur is slow and often takes many years or even decades.

DR. FRED WISE: Dihydrotachysterol has been used with some measure of success in the treatment of pemphigus. It is a question whether the mobilization of calcium by this drug is the chief factor concerned with its therapeutic action in various diseases, among which is scleroderma.

DR. MAURICE J. COSTELLO: When this patient was presented two years ago she was profoundly ill. As a matter of fact, it was the consensus that she would not live long. Whether it is a coincidence or not, there is a definite relationship between the time that dihydrotachysterol was administered and the improvement that followed. The diagnoses of dermatomyositis and scleroderma were not confirmed by biopsy because we thought they were obvious.

I think that Dr. Abramowitz does not give sufficient credit to dermatologists for the extensive medical study given to patients suffering from diseases of the skin that have obscure systemic causation. This patient was studied from every possible angle. The laboratory procedures covered two pages in the ARCHIVES OF DERMATOLOGY AND SYPHILOGY, and there was not one single ray of light obtained from all this. I think that this holds true for many of these diseases, and to my knowledge, dermatologists have not forgotten the systemic background of these conditions.

Lichen Sclerosus et Atrophicus. Presented by DR. JACK WOLF.

L. G., a girl aged 12 years, presented from the New York Skin and Cancer Hospital, was first examined on Sept. 10, 1942. An eruption had appeared about one year previously. Neither the child nor the mother could offer any information as to the course.

On examination she presented isolated grayish black, verrucous and crusted, nummular and lentil-sized lesions on the dorsal aspects of both feet and also along the sides of the feet. Some of these lesions were surrounded by an erythematous halo. Removal of the hyperkeratotic surface revealed a shiny sclerotic-appearing surface. On the anterior aspects of the legs and on the forearms she presented numerous atrophic, shiny, lentil-sized spots, each with one or more black comedo-like cornified granules.

The histologic examination gave results suggestive of a sclerodermatous process. The Wassermann and Kahn reactions were negative.

DISCUSSION

DR. HOWARD FOX: I agree with the diagnosis and think that scleroderma guttatum should be excluded because of the rough surface of the lesions.

Polycythaemia Vera Accompanied by Acne Urticata Polycythemica and Loss of Directional Power in the Fingers of the Left Hand. Presented by DR. MAURICE J. COSTELLO.

F. S., a man aged 40, was first examined by me on Sept. 19, 1942. He stated that he had enjoyed good health until one year previously, when after a vacation in Canada his friends drew his attention to the fact that his eyes were "bloodshot" and his face was "red." He consulted an ophthalmologist, who made the aforementioned diagnosis. His father had died of arthritis, and his mother is living and well. He has two brothers and three sisters who are living and well. He has five children, ranging in age from 1 to 12 years. He does not smoke or drink.

Symptoms of fatigue, headache and disinclination to physical activity have been present for two and a half months. He perspires profusely; sweat can be seen on the body most of the time. In the early part of September a fine, discrete, pruritic papular eruption developed on the face, sides of the neck, upper part of the back, anterior aspects of the shoulders and chest (acne urticata polycythemica). His spleen was barely palpable. Soon after his first visit some loss of directional power in the left hand developed. He was unable to use a typewriter with this hand as formerly because of this condition. Even now, past pointing is feeble when performed with this hand.

A urinalysis performed on Oct. 9, 1942, showed a faint trace of albumin and an excess of indican. The hemoglobin content on September 18 was 148 per cent; on September 19, 142 per cent; on October 2, 135 per cent, and on October 9, 136 per cent. On the last date a complete blood count revealed 7,760,000 erythrocytes and 12,850 leukocytes, of which polymorphonuclear cells comprised 75 per cent, lymphocytes 17 per cent, eosinophils 3 per cent, monocytes 4 per cent and basophils 1 per cent. Treatment has consisted of the use of superficial roentgen rays to the affected areas.

DISCUSSION

DR. GEORGE LEWIS: Polycythemia may be accompanied by a variety of cutaneous manifestations. One of the commonest is rosacea. The development of spider nevi is also common.

DR. DAVID BLOOM: It is my impression that dermatologists are too much awed by the internists, who seek to explain the presence of any cutaneous eruption by a disturbance of internal organs. The fact is that the skin as an extremely complex organ may be disturbed primarily without any other organ harboring the cause of that disturbance. Moreover, it has been shown experimentally (*Jap. J. Dermat. & Urol.* **44**:51 [Aug. 20] 1938) that primary dermatitis may produce disturbance of internal organs. Of course, I do not deny the necessity and value of thorough general examination.

Leukoderma Treated with Intracutaneous Injections of Tyrosinase Enzyme. Presented by DR. HERMAN SHARLIT.

P. G., a Negro woman aged 42, acquired symmetric areas on the thighs about one and a quarter years ago which consisted of oval vitiliginous patches of the size of a silver dollar. These areas corresponded exactly to the rubber guards covering the garter clips on her girdle. The patient used two similar girdles alternately for about one year, at which time she came to the conclusion that the depigmentation was in some way due to the pressure of these garter clips on her skin. Thereafter, while not discarding the girdle or removing the clips, she used circular garters to hold up her stockings.

The patient was first examined on Aug. 26, 1942. The vitiliginous areas were dead white and in striking contrast with the healthy Negro skin surrounding them. At this time she was advised to discard the girdle completely, since it was obvious that the leukoderma was due to an antioxidant in the rubber.

On September 17, a suspension of tyrosinase enzyme was injected intracutaneously into several areas in both patches. One week later bluish gray areas appeared in the patches. Then followed similar injections twice a week in these same areas, with a continued intensification of the pigmentation. I purposely avoided injecting the suspension into the skin at the margin of the lesions, so that the original pallor of the vitiligo could be contrasted with the changes in the parts injected. After the third injection it was noted that the normal skin immediately below the lesion on the left thigh and covering a palm-sized area had become distinctly darker than the surrounding healthy skin.

The lesions at present show a bluish gray color of somewhat uneven intensity which cannot be expressed on pressure and which contrasts rather grotesquely with the color of the normal Negro skin. This color is due to an induced melanin, produced through the action of tyrosinase enzyme. Unfortunately, a biopsy cannot be obtained.

DISCUSSION

DR. E. WILLIAM ABRAMOWITZ: It is interesting that tyrosinase should cause this kind of pigmentation.

DR. HOWARD FOX: Dr. Sharlit has made a commendable attempt to reproduce normal pigment, and it will be interesting to watch the further progress of the patient. Up to the present the cosmetic appearance of the lesion has certainly not been improved.

DR. DAVID BLOOM: I have made injections into a depigmented spot of a patient with vitiligo without obtaining any pigmentation. But injections into the skin of other patients produced slate gray pigmentation which persisted for a few weeks to a few months.

DR. JACK WOLF: I think that Dr. Sharlit's demonstration tonight is extremely interesting. While the treatment should be attempted for patients with vitiligo, the demonstration in leukoderma loses none of its effectiveness and is equally instructive. I was struck by the bluish gray color, which is apparently not in the epidermis but below it. The future developments will be of interest, since Bloch originally contended that dopa-oxidase is not identical with tyrosinase.

DR. MAURICE J. COSTELLO: A physician, at my suggestion, injected into several vitiliginous patches on his body 1 per cent gold sodium thiosulfate dissolved in 2 per cent procaine hydrochloride solution and later exposed the areas to ultraviolet radiation. He was enthusiastic about that treatment for a time. When gold salts are given intravenously, they cause increase of pigmentation, which begins around the hair follicles.

DR. HERMAN SHARLIT: The material used is made from mushrooms, which have a high concentration of the enzyme called tyrosinase. Tyrosinase is an enzyme which can produce melanin bodies when acting on certain chemicals. One of the things it does is to destroy epinephrine. Prof. Nelson, of Columbia, who has been working with this enzyme, finally got it in an almost pure form, and Dr. Schroeder, who became interested in its intravenous use to destroy epinephrine in hypertension, reported that the cutaneous area around the injection always became hyperpigmented.

The reaction in this woman's skin has nothing to do with spontaneous healing, because the pigment is different and it does not look like normal pigmentation. This does not mean that it is not physiologic pigment. The impression we get of the shade of a pigment is due to three important factors: the number of granules, their size and their depth. The artificial manner of its production would assure differences in these factors, making for an unusual shade of pigment.

I am satisfied that we demonstrated in this presentation the production of physiologic melanin by the use of tyrosinase. Therefore, my deduction would be that the leukoderma due to antioxidant is destructive of the enzyme necessary to produce pigment and that tyrosinase may act as an efficient enzyme to supply this loss.

Extensive Postacne Keloids. Presented by DR. FRED WISE.

M. M., a man aged 20, referred by Dr. J. Fleiss, had been afflicted with severe attacks of acne indurata since the age of 13. He was strong and well nourished.

Keloids of varying size and extent developed on all areas where acne lesions had appeared, namely, the cheeks, neck, chest, shoulders and upper half of the back. Those on the back and chest were firm, elevated, closely grouped and sharply marginated, varying in size from 8 to 15 mm.

The most extensive tumors were located on the sides of the neck, over the upper half of the sternocleidomastoid muscles. Here, the individual tumors had become confluent, resulting in the formation of hard, elevated, corrugated, irregularly marginated tumor masses with plateau-like surfaces; these masses measured approximately 3 by 4 inches (7.5 to 10 cm.) in diameter.

He had received roentgen and radium treatments; also surgical measures were tried, but without avail.

DISCUSSION

DR. HOWARD FOX: This patient was under my care for months; some of the largest keloids were treated by electrodesiccation and some by cautery during procaine hydrochloride anesthesia. Some of the keloidal masses were excised by Dr. J. D. Whitham, after which the areas were treated by filtered roentgen therapy. The difficulty in treating this patient was partly due to his lack of cooperation and courage and partly to the extent and severity of the process. These are among the most severe keloids following acne that I have seen.

DR. ANTHONY C. CIPOLLARO: As Dr. Fox said, such lesions are difficult to treat successfully. If this patient had but a single lesion, one of several methods could be used successfully. I think that it is worth while to try treating some of the worst lesions with solid carbon dioxide. When I first heard about this method of treating keloids, I thought that it would cause the lesion to become larger. To my surprise, I found that in many cases treatment with solid carbon dioxide yielded better results than treatment with roentgen rays. The method is practical. Several lesions could be treated at each sitting; hence in the course of many months or a year or two, substantial improvement should result.

DR. DAVID BLOOM: I have employed solid carbon dioxide in treating keloids arising from acne lesions, with good results. However, I am uncertain as to the result in cases of large keloid tumors.

DR. MAURICE J. COSTELLO: I think the suggestion of Dr. Cipollaro is worth following. Seldom does keloid formation ever follow refrigeration with solid carbon dioxide.

DR. GEORGE LEWIS: In a similar case I had good results from the use of solid carbon dioxide. The technic requires the use of firm pressure, and it is usually necessary to repeat the procedure from six to ten times.

DR. E. WILLIAM ABRAMOWITZ: I intended to use solid carbon dioxide because I had treated 2 patients with satisfactory results. As I remember, this boy has received many treatments with radium with no results.

I recall a patient with a naevus pigmentosus who was treated with solid carbon dioxide and for whom that treatment had to be stopped because a keloid developed.

DR. HOWARD FOX: I should like to ask Dr. Cipollaro if he can cause complete and permanent flattening of these large keloids by even a dozen treatments with solid carbon dioxide.

DR. ANTHONY C. CIPOLLARO: My experience in treating keloids with solid carbon dioxide has been so favorable that I prefer it to roentgen irradiation.

DR. HOWARD FOX: Solid carbon dioxide at least will rarely cause keloids. I can recall but a single case in which this occurred. In that case a patient of the late Dr. Ochs suffered from a slight keloid of the face after treatment of a port wine mark.

Black Hairy Tongue. Presented by DR. ANTHONY C. CIPOLLARO.

Mr. A. T., aged 37, presents a lesion of his tongue which he thinks has been present for about two months. During this time he has used a mouth wash, magnesia magma, as a gargle, has taken vitamin B complex and has changed his toothpaste.

His general health is now good, but he had had trouble with his sinuses. He has no subjective symptoms except that when he takes certain foods or drinks an undesirable taste remains many hours afterward. Besides, he does not like the appearance of his tongue.

The patient presents on the posterior aspect of the dorsal surface of the tongue a dark brown V-shaped lesion which seems to be made up of long hairlike structures. Mycologic examination did not reveal the presence of fungi.

The anterior half of the lesion was curetted, and the base was painted with a 1 per cent solution of chromium trioxide.

DISCUSSION

DR. HOWARD FOX: Dr. Herman Prinz, of Philadelphia, who has made a thorough study of lingua nigra, recommended for treatment a 10 per cent solution of salicylic acid in alcohol.

DR. JACK WOLF: I have used mild trichloroacetic acid with excellent results.

DR. FRED WISE: In 2 instances of well developed lingua nigra I had prompt curative results from the application of trichloroacetic acid. Two treatments at fortnightly intervals sufficed.

DR. ANTHONY C. CIPOLLARO: I shall try the method of curettage followed by the application of 10 per cent trichloroacetic acid.

NOTE.—This patient was treated by the aforementioned method, with favorable results. Neither deep curettage nor local anesthesia was necessary.

Lichen Sclerosus et Atrophicus. Presented by DR. JACK WOLF.

R. R., a woman aged 58, first showed signs of the present eruption one and a half years ago. The lesions were profuse from the onset, and only occasional lesions have appeared since then.

The eruption is almost wholly confined to the cubital regions and the flexor surfaces of the wrists and consists of numerous approximately lentil-sized, discrete, flat-topped lesions, some of which are smooth, shiny and slightly depressed while others are slightly elevated, rough and flat. In the main, the former type of lesion is present in the cubital regions and the latter on the wrists. Occasional lesions are also present on the forearms and on the chest. Many of the verrucous lesions present blackish brown cornified comedo-like plugs.

DISCUSSION

DR. WILBERT SACHS: I should like to know whether there are any changes on the vulva, because such lesions frequently are seen associated with Hallopeau's disease. I find atrophy but no sclerosis, though clinically the lesions appear sclerotic.

Dr. Chargin and I have examined many slides, and in none did we find sclerosis.

DR. FRED WISE: Sections examined in the sclerous stage of the papule closely simulate the microscopic changes of scleroderma; when examined in the atrophic stage, the clinically visible atrophy is reflected in the histologic section.

DR. JACK WOLF: This patient has received a total of ten ¼ skin units and has, I feel, been benefited thereby. The lesions are softer than they were before radiation therapy was instituted.

Peculiar Marginal Blepharitis (Due to Yellow Oxide of Mercury?). Presented by DR. DAVID BLOOM.

K. V., a woman aged 25, came to the New York Skin and Cancer Hospital on Sept. 11, 1942, with an eruption on the eyelids of three years' duration.

On examination the edges of the eyelids and the inner canthi were slightly erythematous and thickened, assuming the shape of a cord of the thickness of a pencil. The thickening was undoubtedly due, for the most part, to edema of the tissues. On the lower eyelids there were only a few eyelashes.

The eruption started three years ago, with pruritus of the left upper eyelid which caused the patient to rub her eye frequently. A diagnosis of cyst was made by the attending physician, who incised the left upper eyelid. Later, a stylike lesion developed on the right upper eyelid; yellow mercuric oxide was prescribed. This medication was used by the patient up to three months ago for the thickening of the edges of the eyelids, which has been present for the past one and a half years.

Since Sept. 18, 1942 the eruption has improved considerably owing to the application of boric acid solution and ointment.

DISCUSSION

DR. DAVID BLOOM: The amazing improvement of the eruption within a short time following the application of wet dressings of boric acid solution and boric acid ointment indicates strongly that the application of irritating substances, particularly of yellow mercuric oxide, is the most important factor of the persisting inflammation of the eyelids.

DR. ISADORE ROSEN: I think this patient has more than blepharitis; she has lymph stasis. There is a distinct inflammatory reaction and probably changes in the tissues which have given her a definite lymphedema.

DR. HOWARD FOX: Have any of the members ever seen similar changes in the eyelids from application of yellow mercuric oxide? This drug must be almost entirely harmless to the eyes and eyelids, judging by the enormous usage it has had for years by general practitioners as well as ophthalmologists. It is obviously proper in this case to stop the use of the drug and observe the results.

DR. E. WILLIAM ABRAMOWITZ: Alexander Pagenstecher about 1866 introduced yellow mercuric oxide ointment for the treatment of phlyctenular conjunctivitis and keratitis and not for blepharitis (Hosford, G. N., and McKenney, J. P.: *J. A. M. A.* **100**:17 (Jan. 7) 1933). Removal of the crusts in blepharitis may be accomplished just as well with petrolatum with or without boric acid. There is present a chronic inflammatory process of the lids in which the fibrous tissue or lymphatics participate.

DR. JACK WOLF: I doubt whether this eruption is due to sensitization to mercury. The eruption has remained localized from the beginning. Dermatitis from the application of mercury would also have involved contiguous skin surfaces. The patch test with mercury will, therefore, almost certainly give a negative result. I believe that this is an eruption of unusual character which must remain undiagnosed for the present. I should like to suggest the use of 1 per cent solution of brilliant green (tetraethyldiaminotriphenylmethane sulfate).

DR. MAURICE J. COSTELLO: There is one feature that this patient presents that is not seen in blepharitis, and that is dilatation of the opening of the nasolacrimal puncta of the lower eyelids. I think that the yellow oxide of mercury or the vehicle is causing the blepharitis.

DR. ANTHONY C. CIPOLLARO: I do not think the patient has blepharitis at all. There are no evidences of an acute inflammation. However, there is lymph stasis. I do not know the nature of the pathologic changes, but I do not think that they are due to anything she put on the lids. I think that the eruption could be caused by constant trauma from rubbing and pulling out eyelashes, which the patient admits doing. I suggest that a biopsy be made and that later the lesions be treated with roentgen rays.

DR. GEORGE LEWIS: Would lymph stasis alone account for the alopecia? Would that not require an inflammatory condition? I doubt the statement concerning self epilation.

Epidermolysis Bullosa and Ichthyosis Occurring Simultaneously. Presented by DR. MAURICE J. COSTELLO.

N. A., a boy aged 7 years, from the New York Foundling Hospital, presented soon after birth dime-sized to quarter-sized areas of denudation on the abdomen, back and lower extremities. Bullae containing a straw-colored fluid were present on the pubic region and on the posterior aspects of the thighs. A diagnosis of impetigo neonatorum was made at that time. Staphylococcus aureus was found in the lesions.

The diagnosis of epidermolysis bullosa was not recorded until the child was 2½ years old, when lesions were also found in the mouth. Urethral bleeding was discovered in October 1942, when the child was 7 years old. Roentgenograms of the long bones on Nov. 18, 1938 showed a number of old rachitic lines and a moderately diffused atrophy of all the long bones.

A roentgenogram of the large intestines after a barium sulfate enema showed a moderate degree of megasigmoid. An intravenous pyelogram made on Sept. 18, 1942 showed that the bladder was enlarged and elongated. Its superior portion was drawn upward on the right side and was somewhat elongated, which suggested a congenital anomaly. The oral lesions were found to contain Vincent's organisms on several occasions. This evening he presented two types of eruption. One consisted of numerous pinhead-sized to cherry-sized bullae and areas of denudation interspersed with milia-like retention cysts. The other was a diffuse, large, scaly eruption on the anterolateral aspects of the upper and lower extremities, which was clinically ichthyosis. Superficial white patches were seen on the buccal mucosae, suggesting leukoplakia. Two quarter-sized areas of alopecia were present on the scalp, suggesting a minor congenital ectodermal defect.

DISCUSSION

DR. ANTHONY C. CIPOLLARO: I agree with the diagnosis. There may have been internal disturbance, the nature of which has not as yet been discovered. The face presents an old and shriveled look; the skin is dry and the bullous lesions lead to atrophy and even to well developed deformities. All these signs point to visceral or glandular changes. This patient should be thoroughly studied in cooperation with the department of internal medicine.

DR. HERMAN SHARLIT: I think that in this type of case effort should always be made to get a family history, so that the hereditary background can be completely brought out.

DR. GEORGE LEWIS: There was a café-au-lait spot on the front of the body suggesting neurofibromatosis.

DR. DAVID BLOOM: Cases have been reported in which ichthyosis and epidermolysis bullosa-like lesions were associated. Dr. Cipollaro hopes to find an explanation for the abnormality of the skin in some of the internal organs. I am afraid he will be disappointed. This is an abnormality of the skin the explanation of which is to be found in defective germ plasm.

Ectodermal defect means defect in ectodermal structures based on disturbance in development of the ectoderm which takes place at an early embryonic stage.

DR. J. FRANK FRASER: I should like to ask Dr. Costello whether there is a history of heredity in this case. Ichthyosis is generally regarded as a hereditary disease, perhaps the most hereditary of all diseases. I should also like to ask whether any one knows of a case of the association of these two diseases, ichthyosis and epidermolysis bullosa. I agree with the two diagnoses in this case.

DR. FRED WISE: The term ectodermal defect has been aptly applied to an easily recognized entity; but ectodermal defects play a part in various cutaneous diseases under different designations. Congenital ectodermal defect is an easily recognized disease picture.

DR. MAURICE J. COSTELLO: This is the third patient that I have observed who has had coexisting epidermolysis bullosa and ichthyosis. This boy also has a large sigmoid colon, a peculiar-looking elongated bladder and a large spleen in addition to the urethral anomaly which was mentioned. I think that Vincent's organisms obtained from the oral lesions are probably an infection of the lesions of the mucous membrane associated with the disease in this patient.

Erythema Multiforme Perstans Recurrens and Psoriasis of Palms. Presented by DR. HERMAN SHARLIT.

B. P., a woman aged 63, came to the New York Skin and Cancer Hospital on Sept. 18, 1942, with an eruption on the trunk and extremities of four years' duration and an eruption on the palms of one year's duration.

On the chest, back, thighs and abdomen there are a moderate number of raised erythematous lesions in the form of incomplete circles, which are slightly scaly and associated with mild pruritus.

On the palms and palmar surface of the fingers there are lentil-sized to dime-sized hyperkeratotic plaques with fissuring in some. The nails show transversal striation, splitting at the free margin, pitting and subungual keratosis.

A laboratory examination, including a urinalysis, and a blood count, revealed normal conditions. Biopsy of a specimen from a lesion on the body indicated conditions compatible with erythema multiforme perstans. The Wassermann reaction was negative.

DISCUSSION

DR. HOWARD FOX: A persistent erythema of the chest is the only diagnosis I can make. In regard to the palmar lesions, I should like to ask Dr. Sharlit on what ground he is able to make a positive diagnosis of psoriasis clinically.

DR. E. WILLIAM ABRAMOWITZ: I do not think there is any question about the eruption on the body being erythema multiforme. The keratotic lesions on the palms are possibly arsenical keratoses. The ridging of the nails may be arsenical. The patient probably is or has been coming into contact with arsenic, to which she is susceptible.

DR. GEORGE LEWIS: I should like to offer the suggestion that injections of bismuth be administered, with some hope of at least temporary improvement. Such therapy seems to work almost specifically for patients with such lesions. The palmar lesions impressed me as arsenical keratoses. The patient said that fifteen or twenty years ago she had injections of some undetermined substance, which may have been arsenic.

DR. MAURICE J. COSTELLO: I agree with Dr. Lewis that the administration of bismuth subsalicylate intramuscularly is a treatment well worth trying for the eruption that this patient presents.

DR. JACK WOLF: The palmar lesions do not look like psoriasis, and I hesitate to make that diagnosis in the absence of other cutaneous lesions.

DR. DAVID BLOOM: I am responsible for the diagnosis of psoriasis of the palms which I made on clinical grounds.

In the cases of arsenical keratosis which I have observed the palms and soles presented keratotic verrucous excresences and not the smooth hyperkeratotic lesions seen in this patient. This type of eruption I have seen frequently associated with psoriasis.

DR. WILBERT SACHS: I do not see how one can say whether the small isolated hyperkeratotic lesions on the palms and soles, without evidence of psoriasis in other areas, are or are not those of psoriasis. I think the diagnosis must be made by biopsy.

DR. ANTHONY C. CIPOLLARO: I think that the lesions on the palms are arsenical keratoses and those on the lower extremities are erythema multiforme.

DR. FRED WISE: One variety of keratosis deserving of consideration in differential diagnosis is keratoderma climactericum of Haxthausen.

Myxomatous Degeneration; Synovial Cysts. Presented by DR. GEORGE LEWIS.

S. S., a woman aged 57, has had chronic osteoarthritis for many years. For three years there has been a gradual increase in cutaneous lesions confined to the right hand and forearm up to and including the elbow. Many of the lesions have become progressively harder.

Examination discloses a mixture of soft and firm irregularly shaped masses on the right hand and forearm. There is some redness of the overlying skin. Some lesions appear bound down to underlying tissue. The surface of the skin over some of the lesions shows milium-like, pinpoint elevations.

The biopsy shows that diffusely scattered throughout the cutis are numerous myxomatous cells in which little but nuclei can be seen and which have characteristic amorphous tails. These appear to lie free in vacuolated spaces which are separated by gray filmy shreds of tissue. The fibrous tissue stroma has been largely replaced by this myxomatous tissue and appears to be broken up. The myxomatous reaction is rather more diffuse than it would be if this were a circumscribed nodule or tumor. Roentgen studies revealed a substernal thyroid, an enlarged heart, normal pulmonary fields and arthritis of the hand. The Wassermann reaction was negative.

DISCUSSION

DR. FRED WISE: The formation of tumors as presented by this patient is the first instance of its kind to come under my observation.

DR. GEORGE LEWIS: It is possible that the degenerative process is due to the outpouring of synovial fluid into the subcutaneous tissues and that this material has acted as the causative agent. In this particular case the myxomatous degeneration apparently was not a localized process in the cysts but even from the start was rather diffuse.

A Case for Diagnosis (Erythema Nodosum?). Presented by DR. GEORGE. M. LEWIS.

M. R., a man aged 46, an engineer, complained of the development of crops of lumps in the skin during the past year and a half. His general health has been excellent except for headaches, for which he took enormous doses of salicylate compounds over a period of one year just prior to the onset of the eruption. The first cutaneous lesion was a small elevation on the left thigh. The area spread peripherally, became hard and finally involved almost the entire thigh. Itching was troublesome. After three weeks, the swelling subsided, finally disappearing after undergoing softening which the patient likened to a "flabby bag of water." No scarring remained at the site. In a few weeks, a similar lesion occurred on the right leg. He was then free of lesions for three months. However, at irregular intervals since then, lesions of various sizes have appeared. Two thirds of them have occurred on the legs and thighs. During the past eight months there has been no interval of freedom. Since he has used ointment of benzoic and salicylic acid N. F. on his feet, many new lesions have appeared.

Examination shows a somewhat obese man who does not appear seriously ill. There is one large indurated plaque on the right thigh in which the skin is of cartilaginous hardness. There were several smaller firm, dull-erythematous lesions on the legs and back. There is a dermatophytosis of the soles and toe nails, the appearance being typical for Trichophyton purpureum.

The Wassermann reaction was negative, the urine normal and the blood count normal except for 11 per cent eosinophils; three cultures of blood gave negative results; examination of the stool showed no parasites, and no salicylates were found in the urine. The sputum did not contain tubercle bacilli. The corrected sedimentation rate was 0.7. Cultures of scrapings from the feet revealed Trichophyton purpureum. There was no local reaction to trichophytin. Roentgenograms of the chest were normal. Fungous and bacteriologic cultures from a biopsy specimen of a new lesion did not grow any pathogenic organisms. The histologic section showed a diffuse perivascular infiltrate, largely lymphocytes and polymorphonuclear leukocytes.

DISCUSSION

DR. GEORGE LEWIS: There were two roentgenograms of the chest, one showing a vague sort of shadow which could not be interpreted and the second one, made ten days later, showing no abnormal shadow. Erythema nodosum was considered for want of a better diagnosis, but I am fairly certain that it is not the correct one. It is interesting that after the patient's feet were treated more lesions developed. Attempts to correlate the Trichophyton purpureum infection with the eruption have so far been fruitless.

DR. HOWARD FOX: The complete absence of pain and tenderness and the duration of the lesions exclude erythema nodosum. The long duration also excludes giant urticaria. I think it is simply an unusual type of persistent erythema of unknown cause.

DR. E. WILLIAM ABRAMOWITZ: This eruption belongs to the erythema nodosum–like lesions of erythema multiforme.

DR. JACK WOLF: This is a very unusual case. I do not know what the diagnosis is, but there is no resemblance to erythema nodosum tonight.

DR. DAVID BLOOM: This patient presents at the inner aspect of the left knee a definite ring with a hard border which consists of nodules. This conforms with the appearance of toxic persistent erythema.

DR. ISADORE ROSEN: This patient presents one feature which is evident, namely, an old dermatophytosis of the feet. I should like to associate the erythema nodosum with this infection. One occasionally sees all types of cutaneous manifestations, from mild erysipelas-like infections to extensive generalized eruptions which may resemble various dermatoses caused by fungous infections of the feet. These frequently lead to confusion and difficulty in diagnosis and treatment.

Lymphoblastoma Resembling Neurodermatitis. Presented by DR. E. WILLIAM ABRAMOWITZ.

M. L., a man aged 47, came to the New York Skin and Cancer Hospital on June 29, 1942, complaining of a generalized pruritic eruption of one year's duration.

On examination the skin appeared hyperpigmented and lichenified, with numerous crusted excoriated lesions and scars. Large lymph glands were present in the axillary and inguinal regions.

The urine was normal. A roentgenogram of the lungs showed productive tuberculous infiltration in the upper lobe of both lungs with secondary bronchial dilatation and retraction. Blood count on August 9 revealed: erythrocytes, 2,870,000; hemoglobin content, 57 per cent; color index, 0.98; leukocytes, 17,500; neutrophils, 51 per cent; eosinophils, 18 per cent; monocytes, 8 per cent, and band forms, 5 per cent. Histologic examination of the skin showed lymphoblastoma.

DISCUSSION

DR. DAVID BLOOM: I think it is important to determine whether the infiltration in the lungs diagnosed as tuberculous may not possibly be due to lymphoblastoma or to Hodgkin's disease, in view of the fact that in this patient tubercle bacilli have never been found in the sputum.

DR. MAURICE J. COSTELLO: I think that when a patient presents an eruption such as this, a universal, hyperpigmented, extremely pruritic eruption with many scratched papules, the diagnosis of Hodgkin's disease should always be entertained. This is especially so if there are no periods of remission in the pruritus. I presented an elderly woman last year, and all the members commented on the severe degree of hyperpigmentation of her skin. The final diagnosis of Hodgkin's disease was made when an enlarged lymph node which revealed the characteristic histologic picture was removed from her neck. The diagnosis of Hodgkin's disease is difficult to confirm when the manifestations are chiefly cutaneous. Study of the blood cells and sternal marrow cells seldom throws light on the diagnosis. It is better to remove a lymph node and study its histologic structure.

DR. HOWARD FOX: Every dermatologist encounters cases like this in hospital practice and is rarely in a position to make more than a tentative diagnosis of lymphoblastoma. The eruption is apt to be universal and to show pigmentation and intense thickening of the skin. As a rule, until the terminal stage, no diagnostic aid is given by a blood count or by biopsy of lymph nodes. Eventually, either leukemia or Hodgkin's disease is apt to appear.

DR. FRED WISE: As an aid in differential diagnosis, I suggest a punch biopsy of the sternal marrow.

Basal Cell Epithelioma. Presented by DR. JACK WOLF.

G. S., a man aged 79, presented himself at the New York Skin and Cancer Hospital on Sept. 8, 1942, with a history of an ulcerating lesion on the back of fifteen years' duration. The lesion had never been treated.

On examination he presented a tremendous ulcer in the interscapular region extending from the first dorsal to about the seventh dorsal vertebra, roughly oval and 4 inches (10 cm.) in

width at the middle. Muscle tissue was invaded and exposed. Surrounding the entire lesion was a shiny, elevated, pale yellow, cordlike border. The base was not indurated. Histologic examination confirmed the clinical diagnosis of basal cell epithelioma.

There has been considerable improvement since roentgen therapy was instituted.

DISCUSSION

DR. ANTHONY C. CIPOLLARO: This is the most extensive basal cell epithelioma that I have ever seen. It is remarkable how a person could neglect such a large ulcer for such a long time. Clinically and histologically the lesion is a basal cell epithelioma. It is responding to treatment with roentgen irradiation, just as one would expect such a lesion to respond. This patient has been under treatment for the past three weeks, and during this period he has received a total of 12 erythema doses of roentgen rays. Unfiltered low voltage (100 kilovolts) radiation was used. A total of 3,600 r has been administered. Because of the immense size of the lesion only one half at a time was exposed in order to obtain equal distribution of radiation. There is already at least 50 per cent improvement.

DR. HOWARD FOX: It is extraordinary to see such a large excavation in a basal cell epithelioma. The only other possible diagnosis would be syphilis. This, however, could be excluded by the lack of a punched-out and festooned border and by the lack of any spontaneous healing in the course of fifteen years. The negative serologic reaction also speaks against syphilis.

DR. E. WILLIAM ABRAMOWITZ: Only a few days ago I saw a patient with a coconut-sized epithelioma on the left temple who received low voltage unfiltered roentgen treatment (about 4,500 r in six weeks) with excellent results.

DR. WILBERT SACHS: If the biopsy reveals a basal cell epithelioma, there can be no further doubt. However, I strongly suspect that in a lesion present for fifteen years somewhere in that border there is also a prickle cell epithelioma.

DR. JACK WOLF: I agree that many of these long-standing basal cell epitheliomas eventually show histologic changes either of basosquamous or of squamous cell epithelioma. However, I did not see any such changes in the section I studied. In spite of the extent of the lesion, the peripheral portion presented the typical elevated, shiny border of basal cell epithelioma before radiation therapy was instituted.

FRED WISE, M.D., *President*

ANTHONY C. CIPOLLARO, M.D., *Secretary*

November and December 1942

Vitiligo Treated with Tyrosinase. Presented by DR. HERMAN SHARLIT.

P. G., a woman aged 42, was presented at the October 1942 meeting of this society (p. 430).

DISCUSSION

DR. HERMAN SHARLIT: It may be recalled that in this patient symmetric areas of leukoderma developed under the rubber guards covering the garter clips on her girdle, and I felt satisfied that they were acquired leukoderma due to the antioxidant in the rubber. Usually a patient with such an eruption gets well after she is relieved of the irritant. I am presenting this woman today to show that the natural pigmentation is coming back. Whether the treatment hastened its return or not, I do not know. I think this therapy should be tried for the different kinds of vitiligo in the hope that it may prove to be a good method of treatment. If one person alone uses it, a determination of its value will be long delayed.

DR. DAVID BLOOM: I have observed the same sort of pigmentation when I injected tyrosinase into vitiliginous skin. Microscopic examination of such pigmented skin did not reveal any iron or any melanin granules in the basal cell layer. Thus, the nature of this pigmentation is unknown. It is perhaps due to the cellular infiltrates which are present throughout the whole corium.

Intradermal injection of tyrosinase produces in normal and in abnormal skin a persistent wheal, erythema and this peculiar pigmentation.

DR. WILBERT SACHS: I refer not to the small pigmented macules, which are probably melanin, but to the grayish blue spots. The Perles reaction was negative, showing that whatever it was that gave the color to the lesions it was not iron pigment.

DR. E. WILLIAM ABRAMOWITZ: Have injections of isotonic solution of sodium chloride been used as a control?

DR. HERMAN SHARLIT: Control injections of isotonic solution of sodium chloride have not been tried. If one starts with that type of control, one might just as well use anything ever heard of. An isotonic saline solution should produce no reaction; it is not an irritant. Tyrosinase is an irritant. There is a strong cellular reaction in the tissue from it. One can see the immediate reaction from the injection given this morning.

This is physiologic melanin in the sense that the color is produced by the body, although it may not be the kind of melanin the body ordinarily makes, unless these pigmented granules are so small that they are not revealed by the microscope. One gets the impression of the color only when a gross picture is obtained. Under the microscope nothing is seen other than a cellular reaction.

One of the characteristics of vitiligo is that it does not react to irritation. Ultraviolet irradiation produces no effect. I know that irritants have been used in treatment of vitiligo in the hope that they would stimulate pigment formation.

As far as I know, this is the first attempt to produce pigment in a vitiliginous skin. The material used is made by the Upjohn Company, and it can be obtained from the manufacturers.

This is not a particularly good case for study, because the patient should spontaneously get well. Dr. Bloom is working on spontaneously acquired leukodermas and vitiligo, and if he succeeds in inducing normal pigmentation that will be meaningful. A single injection of tyrosinase brings a bluish color to the skin after forty-eight hours.

DR. WILBERT SACHS: At the time I saw the slide the cellular reaction was so great that I suggested that this bluish gray color might be due to the densely packed cellular elements. Since I saw no evidence of melanin and no iron pigment, I did not believe it was due to pigment.

A Case for Diagnosis (Lichen Planus? Pityriasis Rosea? Eczema?). Presented by DR. JACK WOLF.

S. I., a man aged 24, presented himself at the New York Skin and Cancer Hospital on Nov. 10, 1942, with a widespread eruption most pronounced on the torso, the upper extremities and the neck. On the neck the eruption consisted of numerous irregularly shaped, small, violaceous-tinged, rough, dry maculopapules with a tendency to confluence. On the chest the eruption was sparse and consisted of numerous pinhead-sized papules and macules of similar character; on the upper extremities the lesions were somewhat larger. Plaquelike lesions were present on the shoulders. The small scaly lesions on the chest, running along the lines of cleavage, suggested pityriasis rosea. Small erythematous lesions were also present on the penis, buttocks, thighs and legs.

NOTE.—Within several days after this patient was presented the characteristics of the eruption had entirely changed. It no longer resembled lichen planus, and the clinical picture was that of an eczematous dermatitis. The histologic picture was that of a toxic dermatitis. Within three weeks the eruption had entirely disappeared.

DISCUSSION

DR. E. WILLIAM ABRAMOWITZ: I recall the case of a private patient with a similar eruption. The first time I saw him I thought he had pityriasis rosea. The next time I saw him, the eruption was beginning to look like lichen planus. After several return visits I made up my mind that it was an unusual type of fine papular eczematous eruption. This was confirmed later by a biopsy. I think this patient has a peculiar form of lichenified or small papular eczema, and perhaps, as in my patient, it may prove to be due to inhalation of pyrethrum. There was also a positive reaction to a patch test. It took a long time for the eruption to disappear.

DR. GEORGE LEWIS: I am in favor of a diagnosis of lichen planus in this case. All dermatologists have seen instances of lichen planus in which the eruption simulated pityriasis rosea at first, afterward becoming typical for lichen planus. The violaceous color, the presence of an occasional flat-topped papule, the atypical distribution for pityriasis rosea and the presence of lesions on the penis are points in favor of lichen planus.

DR. HERMAN SHARLIT: I agree with Dr. Lewis. In some of the areas the lesions assume a circular configuration; this is a further confirmation of the diagnosis lichen planus.

DR. MAURICE J. COSTELLO: I agree with Dr. Lewis. I have seen several patients at the Academy of Medicine in the last four or five years with eruptions that appeared to be pityriasis rosea in the beginning but eventually became lichen planus. The eruptions occurred during the course of arsenic therapy for syphilis. Eruptions of this sort first resemble pityriasis rosea, later psoriasis and finally lichen planus, even to the appearance of lesions on the mucous membrane.

DR. DAVID BLOOM: I agree with the previous speaker, but for a definite diagnosis the help of a pathologist is needed.

DR. PAUL E. BECHET: I should like to ask Dr. Wolf if the patient has recently been given any of the heavy metals. I have noted eruptions from arsphenamine so closely resembling lichen planus or pityriasis rosea as to be clinically indistinguishable from them. In an instance that I remember, a patient presented both types of lesions after the use of a gold compound in the treatment of lupus erythematosus of the scalp.

DR. M. B. PAROUNAGIAN: Clinically I agree with Dr. Lewis. I think the eruption looks like lichen planus.

DR. J. FRANK FRASER: I agree with Dr. Lewis' interpretation of the case. To my mind the distribution is against the diagnosis of pityriasis rosea. One does not see pityriasis rosea on the lower extremities, and the fact that there are lesions on the glans penis is also against the diagnosis of pityriasis rosea. I do not think that itching is significant one way or another. The lack of itching would not exclude the diagnosis of lichen planus in this case. I think that eventually it will be found that in this case lichen planus will develop even though one cannot see any typical lesions of that disease tonight.

Erythema Nodosum (Cold). Presented by DR. GEORGE M. LEWIS.

A. J., a housewife aged 32, was first seen in the dermatologic clinic of the New York Hospital on Oct. 28, 1942. During the winter of 1937-1938 painful red lesions developed on the backs of the legs above the ankles. The lesions persisted until spring, when they spontaneously disappeared, leaving bluish discolorations. Similar lesions reappeared on the legs the following winter and each winter since then, with the same tendency to disappear with the onset of warm weather. The lesions are painful on exposure to cold or during wet weather and also cause a certain amount of disability, making it difficult for the patient to carry on her housework. Last winter the lesions developed as usual but lasted longer than on previous occasions, some being present until June. There has been the customary appearance of the disease this fall. The legs are chiefly affected. A solitary lesion was noted on the left arm.

Examination discloses several subcutaneous swellings below both knees. The lesions are freely movable. The skin overlying them is not altered except that it is reddened in a few areas. A bluish discoloration marks the sites of older lesions.

The Wassermann reaction was negative Biopsy of an early lesion showed a localized cuff of lymphocytic cells surrounding the majority of vessels in the upper and middle layers of the cutis. There was a leukocytic thrombus in an occasional vessel, and there was dilatation of the lymph spaces.

DISCUSSION

DR. ANTHONY C. CIPOLLARO: This is a difficult eruption to diagnose. This patient presents features of both erythema nodosum and erythema induratum. However, the history and clinical signs favor the diagnosis of erythema nodosum. It may be due to a hidden focus which has not been discovered so far.

DR. MAURICE J. COSTELLO: I think this patient has recurrent erythema nodosum which is precipitated by cold weather. Seven or eight years ago there were two severe winters in succession in New York, and I saw a number of patients at Bellevue Hospital who had an eruption similar to the one this patient presents. The bluish-red painful lesions occurred on the legs on very cold days, and they disappeared as the weather moderated. There may be some focus of infection, tuberculous or otherwise, but I think the precipitating factor is cold weather.

DR. WILBERT SACHS: I do not believe these lesions are unusual. Several years ago in the New York Skin and Cancer Hospital there was a series of patients, chiefly young women, with a similar eruption. This patient gives a definite history that the lesions appear in the winter and disappear in the summer. I do not understand what focus of infection would come only in the winter and not in the summer. This eruption to me is pernio, and while the biopsy shows little, that is the picture one finds in pernio. There is no evidence of erythema nodosum or erythema multiforme. The pathologic picture fits in well with pernio. This may occur anywhere on the body.

DR. E. WILLIAM ABRAMOWITZ: The classic picture of erythema nodosum does not appear to be present. The patient has an irregular distribution of the nodose lesions. One lesion on the elbow disappeared rather quickly. There has not been much extremely cold weather yet. I think this patient should be investigated further. It may be that some other cause may be determined. I do not think that the weather is entirely responsible, but possibly it causes the lesions to persist.

DR. HERMAN SHARLIT: I always had the impression that in the formation of such lesions there is an unusual transudation of fluid, after which the leg gets larger. I have also the impression that these eruptions occur in girls, mostly in Italians. The fluid is drawn into the tissues, and it comes and goes quickly. One can call it erythema nodosum, since certain localized lesions are so edematous that they look like localized infiltrations. The amount of cellular infiltration does not explain the lesions. There is considerable serum. Why not consider these eruptions as allergies, particularly when the reaction is transmission of fluid?

DR. J. FRANK FRASER: I was unable to make a histologic diagnosis, and I suggest that Dr. Lewis perform another biopsy on a specimen from deeper in the lesion. The lesions of both erythema nodosum and erythema induratum are usually found in the deeper layers of the skin and in the subcutaneous tissues. From the history and the pain on pressure, I am more inclined to favor the diagnosis of erythema nodosum.

DR. GEORGE M. LEWIS: It is to be hoped that hospitalization of this patient can be arranged, so that the factors involved in the causation can be more closely studied.

DR. MAURICE J. COSTELLO: I think that proper support of the blood vessels of the lower extremities by rest in bed or by use of suitable bandages and moderate warmth will cause the eruption to clear.

Lymphangioma Circumscriptum. Presented by DR. MAURICE J. COSTELLO.

P. P., a man aged 26, has had an eruption in the suprapubic region for the past ten years. It consists of numerous shiny pinhead-sized to pea-sized honey-colored thick-walled vesicle-like lymphangiectases which empty when compressed and promptly fill again when the pressure is released. The lesions arise from a palm-sized irregularly surfaced erythematous hyperpigmented area. The eruption causes the patient no serious inconveniences.

There is no family history of a similar eruption, but one of the patient's first cousins was born with a spontaneously amputated hand and another has a peculiar congenital anomaly

DISCUSSION

DR. E. WILLIAM ABRAMOWITZ: This eruption is unusual, not only on account of the erythema and the type of vesicles but on account of the slight brownish pigmentation. The patient says that he has not applied anything, but I think something is superimposed on the original condition.

DR. DAVID BLOOM: I agree with the diagnosis. The unusual feature in this case is the location.

DR. GEORGE M. LEWIS: I agree with the diagnosis, but I think the case presents unusual features. There appears to be infiltration at the base, suggesting a low grade infection.

DR. PAUL E. BECHET: I agree with the diagnosis. An unusual feature is the complete absence of blood in the lesions. Most of the lymphangiomas I have observed have contained blood. The location of the lesion on Dr. Costello's patient, the swimming trunk area, is, in my experience, its favorite site. So commonly has this occurred that I have often speculated on the reason for it.

DR. ANTHONY C. CIPOLLARO: I agree with the diagnosis, and I think the redness is due to lymph stasis in the whole general area. My advice is to leave it alone, but if the patient insists on treatment I advise radical surgical removal followed by plastic repair.

DR. MAURICE J. COSTELLO: I thought that tonight I presented a patient with angioma circumscriptum in a form seldom seen, unmarred by trauma and secondary infection. It is in an area where cysts have little chance to be ruptured. When it is in some other location, like the buttocks or the lumbar region, it is frequently subjected to trauma. In such a location the cysts are broken and do not present an appearance similar to that of the eruption in this patient. The problem in this disease is treatment. I recall several patients who were treated with improvement by use of roentgen rays. If inadequate treatment or inadequate surgical measures are used, the patient's plight will be worse, because then he will suffer from chronic lymph stasis.

DR. MAX SCHEER: There is objection to high voltage roentgen therapy because it might injure the bladder.

DR. E. WILLIAM ABRAMOWITZ: Radium has been tried, with no results.

DR. PAUL E. BECHET: Has any one an explanation for the fact that this disease so frequently is limited to the trunk area? The large majority of patients I have seen at different societies have had the lesions on the trunk.

Lichen Nitidus. Presented by DR. GEORGE M. LEWIS.

L. F., a schoolboy aged 7½ years, is presented from the New York Hospital. Five months ago there was an abrupt onset of a rash, which soon became generalized. There has been slight pruritus, noted particularly when he was undressing.

Examination revealed a generalized eruption consisting of discrete skin-colored shiny dome-shaped pinhead-sized papules.

Biopsy revealed changes consistent with lichen nitidus. A roentgenogram of the chest was normal. The reaction to tuberculin was negative. The Wassermann reaction was negative. Examination of the urine revealed values within normal limits. There was no family history of tuberculosis.

DISCUSSION

DR. MAURICE J. COSTELLO: I agree with the diagnosis.

DR. WILBERT SACHS: I agree with the diagnosis. I recall seeing 2 or 3 patients with eruptions just like this, and it so happens that all of the eruptions that were generalized were in children. I wonder if this has been the experience of others.

As to a tuberculous causation, I believe Pincus retracted the statement that such eruptions are of tuberculous origin. In my opinion none of them are tuberculous. Pincus seemed to agree with that.

DR. E. WILLIAM ABRAMOWITZ: I agree with the diagnosis. I recall seeing this patient in the hospital. There has been considerable improvement since then. I also obtained a history that the eruption followed the injection of bismuth, but I do not think it is a bismuth eruption. Eruptions from bismuth are rather infrequent.

DR. GEORGE ANDREWS: I have a patient who has a fairly widespread eruption of lichen nitidus. The eruption is a little more patchy and eczematized than that of this patient, but there are typical lesions on the penis and arms.

DR. J. FRANK FRASER: I never saw lichen nitidus so widely distributed as it is on this patient. Nevertheless, I am unable to entertain any other diagnosis. To my mind the lesions are typical of lichen nitidus. Therefore, I agree with the diagnosis of Dr. Lewis.

DR. L. VAN DYCK: I agree with the diagnosis.

DR. GEORGE M. LEWIS: The unusual feature in this case is the extensive distribution. The cause is often considered to be tuberculosis, but in the few cases I have observed tuberculosis has not been proved to be a factor. Treatment with gold salts is mentioned favorably.

A Case for Diagnosis (Fixed Drug Eruption?). Presented by DR. DAVID BLOOM.

U. S., a Negro woman aged 31, came to the New York Skin and Cancer Hospital on Nov. 9, 1942 with an eruption on the neck, scalp and face of five years' duration.

The eruption on the back of the neck consists of two plaques which are irregular in shape and composed of lentil-sized shiny violaceous papules. The lesions in the middle of the forehead consist of an irregularly shaped, sharply defined thickened hyperpigmented plaque with a bluish tinge. Annular plaques are present on both temples. On the front of the neck there is an erythematous slightly lichenified plaque. The eruption is associated with severe pruritus. The lesions on the back of the neck have not disappeared since their appearance, five years ago, while the lesions on the temples and the anterior aspect of the neck have disappeared and recurred.

The patient gives a history of having taken feen-a-mint (a laxative containing phenolphthalein) six months ago for the last time, while previously she had taken it once every two months for four years.

A Wassermann test made one year ago was said to have elicited a negative reaction.

DISCUSSION

DR. E. WILLIAM ABRAMOWITZ: The patient is taking several drugs, each of which could cause the pigmented eruption on the forehead. There is no definite history of recurrence in situ; instead there is lichenification of the back of the neck, with itching. I should call this not a fixed drug eruption but a localized neurodermatitis.

DR. M. B. PAROUNAGIAN: The lesion on the neck impressed me as being lichen planus. There are shiny papules, and the neck is a rather common location for this disease.

DR. JACK WOLF: I favor the diagnosis of fixed drug eruption. By being scratched and rubbed these lesions have become hyperpigmented, thickened and lichenified.

DR. GEORGE M. LEWIS: I believe the patient has two different diseases. The eruption on the neck impressed me as being typical of neurodermatitis of the localized form. The lesions on the forehead are circinate; they are not elevated; there is no lichenification, and because of their nonspecific appearance they suggest a fixed drug eruption.

DR. VAN ALSTYNE H. CORNELL: I think that the lesions on the back of the neck are typical of neurodermatitis, but the lesion on the forehead, which appeared much later than the others, certainly looks like a drug eruption. The patient says that she has taken feen-a-mint but that so far she has not reacted to phenolphthalein.

DR. MAURICE J. COSTELLO: I think that both lesions are of the same causation. I believe that this patient has a fixed drug eruption—the halo of hyperpigmentation certainly suggests it. In addition, she gives a history of taking headache powders which I think contain acetanilid.

DR. FRED WISE: I regard the eruption as one caused by the ingestion of drugs. In eruptions caused by phenolphthalein, I have noted late changes which simulate eczema and lichenification as secondary phenomena. A young Negress with such an eruption on the back had been under the care of Dr. Abramowitz.

DR. J. FRANK FRASER: I agree that in all probability this is a fixed drug eruption. The lesion on the forehead is rather characteristic, but the lesions on the neck are typical of localized neurodermatitis.

DR. HERMAN SHARLIT: The diagnoses offered are fixed drug eruption and neurodermatitis. One is an etiologic and the other a morphologic diagnosis. They are probably both correct.

DR. DAVID BLOOM: The plaques on the back of the neck have been present for the past five years without any change, while the plaques on the face are of four months' duration. The former lesions look like lichen chronicus simplex, while those on the face appear like a fixed drug eruption. The patient admitted having frequently taken acetanilid-containing powders for headaches. She will be tested for sensitivity to acetanilid.

Persistent Marginal Blepharitis (Due to Yellow Mercuric Oxide?). Presented by DR. E. WILLIAM ABRAMOWITZ.

M. P., a Negro woman aged 48, previously presented at the Bronx Dermatologic Society (Oct. 22, 1942), came to the New York Skin and Cancer Hospital on Nov. 4, 1942, complaining of swelling of the eyelids of eight months' duration. The left upper eyelid showed cord-like thickening and considerable ulceration. The inner portions of the right upper and lower eyelids were similarly affected but to a lesser degree.

The patient stated that about eight months previously the right upper eyelid began to itch. She was treated at an ophthalmologic clinic until recently with yellow mercuric oxide ointment. The pruritus persisted, and ulceration of the eyelids developed. (Further examination revealed destruction of the uvula, with scarring. There was no history of syphilis or tuberculosis or treatment for these diseases. The Wassermann reaction was negative.)

After application of boric acid solution and boric acid ointment the eruption improved considerably within a short time; the thickening diminished, and the ulceration almost disappeared.

A tuberculin test with a 1 to 10,000 dilution gave a 1 plus reaction. A patch test with yellow mercuric oxide on the back of the trunk gave a negative reaction.

DISCUSSION

DR. GEORGE LEWIS: I understand that there has been considerable improvement, and I think that is in favor of the diagnosis as presented. However, there is still a great deal of swelling of the lids.

DR. DAVID BLOOM: This is the second patient shown here with this peculiar marginal blepharitis. The history of the case and the fact that improvement took place after application of a bland ointment suggests strongly that yellow mercuric oxide is probably an important factor in the persistence of the pruritus and the chronic injury produced by rubbing of the eyelids.

DR. HERMAN SHARLIT: In regard to yellow mercuric oxide, I have been advised that microscopic examination of some samples of this ointment clearly showed sharp mercuric oxide crystals. If that is true, most persons who use this product are really rubbing in something that has sharp edges, and there may be a mechanical background in the causation.

DR. WILBERT SACHS: Blepharitis, in my opinion, is an inflammatory process. I was told that there is some hyperplastic tissue here, and therefore I do not believe the eyelids will go back to normal. It is possible that the hyperplasia is due to the mechanical factor involved. If there is fibrosis, there will be some enlargement of the eyelids which will never disappear.

DR. JACK WOLF: The patient presented a month ago and the one presented tonight are being accepted as having the same disease. However, I think the clinical pictures of the 2 patients differ materially and that the diagnoses should be different. The patient previously shown presented a most unusual picture, with erythema and sharply localized rounded, rolled swelling of the torsal margins. The patient presented tonight shows none of these characteristics. The process is suppurative. Exactly what the eruptions which these patients present are, I am unable to say. The eruption in both of these cases is attributed to the yellow mercuric oxide, and yet both of the patients used the mercuric oxide to treat an existing eruption. They were not made worse by the treatment. Further study of these eruptions is necessary. The etiologic role played by the yellow mercuric oxide, if any, remains to be proved.

DR. FRED WISE: I agree with the opinions expressed by Dr. Wolf. When I examined this patient several weeks ago, the lesions on the eyelids simulated an ulcerative tuberculid. I believe that the eruption appeared before the use of yellow oxide of mercury ointment and that the ointment aggravated an already existing pathologic change.

DR. DAVID BLOOM: When this patient was presented before the Bronx Dermatological Society, Dr. Rosenthal cited Hosford and McKenney (*J. A. M. A.* **100**:17 [Jan. 7] 1933), who called attention to the insolubility of yellow mercuric oxide and stated that they had seen granules of yellow mercuric oxide with the slit lamp.

DR. E. WILLIAM ABRAMOWITZ: This is the second case of its kind presented in recent months. Ophthalmologists and others use the yellow mercuric oxide ointment for blepharitis, whereas it was originally introduced for the treatment of phlyctenular conjunctivitis and keratitis. The ointment is put up in tubes by a number of concerns, and I should not be surprised if some crystals are present in the product.

It is a question whether the eruption is due to mercury or to the vehicle, but inasmuch as the vehicle generally consists of petrolatum and perhaps a little wax or hydrous wool fat I doubt whether it is due to the vehicle. It is probably due to the yellow mercuric oxide itself. Undoubtedly these patients have some itching of the eyelids and rub them frequently; this rubbing plus the mercuric oxide may account for the thickening that develops. Improvement occurs after use of the ointment is discontinued and plain borated petrolatum is used.

CHICAGO DERMATOLOGICAL SOCIETY

MICHAEL H. EBERT, M.D., *President*

MARCUS R. CARO, M.D., *Secretary*

Feb. 17, 1943

A Case for Diagnosis (Parapsoriasis?). Presented by DR. THEODORE CORNBLEET, and (by invitation) DR. HENRY C. SCHORR.

C. L., a white girl aged 18, has had an eruption for one month which began on her neck and then became generalized.

The eruption consists of scaling maculopapules. The lesions are superficial and ill defined and have a dry whitish thin scale, in some places simulating that of psoriasis. The scales are easily detached and somewhat powdery on grattage. Capillary bleeding is absent. The epitrochlear glands and superficial chains are not palpable. There are one or two lesions on the face; there are none on the hands and feet or below the knees. The oral mucous membrane is mildly injected, and there is dilatation of its capillaries. The tongue is somewhat inflamed and shows enlarged papillae over the dorsum and especially toward the tip. There are no

subjective symptoms, and the patient's health has been good. There is a moderate cutis marmorata of the wrists, hands and lower extremities.

The Kahn reaction was negative.

DISCUSSION

DR. M. J. REUTER, Milwaukee: I suggest as a possible diagnosis pityriasis lichenoides et varioliformis acuta. There are no vesicles and no scars, but I noted on the sides of the trunk crusted papules which looked as though they might become scarred on healing.

DR. F. E. SENEAR: I thought of pityriasis lichenoides et varioliformis acuta as a strong possibility. I did not think the eruption was pityriasis lichenoides chronica. I think it would be difficult to make that diagnosis for a disease present only for a month. I could find no scales of the "powdering" type one would expect on grattage in that disease. I feel that this patient has a relatively mild form of the disease, as Dr. Reuter said, and there is nothing particularly varioliform about the eruption. One might think of an atypical pityriasis rosea. There were some suggestive lesions on the legs and on the ankles. Prompt disappearance may be expected in the course of the next two or three weeks if it is that disease; Haberman's disease would not disappear so quickly.

A Case for Diagnosis (Erythema Nodosum? Erythema Induratum?). Presented by DR. J. H. MITCHELL and (by invitation) DR. R. L. KESLER.

Mrs. R., a trained nurse aged 29, was first seen on Feb. 6, 1943, with a large erythematous swelling about the left ankle. It had been present for two and one-half years. No injury of any kind preceded the onset. There had been exacerbations and remissions. She was given fourteen roentgen ray treatments, followed by disappearance of the lesion. The diagnosis at that time was streptococcic infection. In August 1942 there was a sharp recurrence, and four more roentgen ray treatments were given at the Cook County Hospital. The condition has persisted since then without remission. Treatment with diathermy and ultraviolet irradiation has been given, without benefit. In 1938 a Mantoux reaction was so violent that the patient was advised never to submit to another test.

On February 6, there was a large, poorly defined area of pitting erythematous edema involving the whole left ankle, with a greater amount of involvement on the inner side. On the shin there was considerable exfoliation, which the patient stated was present before diathermy had been given. The patient was referred to Dr. Kesler, whose report is presented. She has received two intravenous injections of sodium tetrathionate, with remarkable improvement. Examination on February 17 showed an exacerbation which had been present since the preceding day.

DISCUSSION

DR. H. R. FOERSTER, Milwaukee: I do not know how to diagnose the eruption in this case. The lesions are of the erythema nodosum type but are atypical in distribution. They began in the summer, and there does not appear to be a superficial disturbance of the peripheral circulation of the toes and dorsum of the foot; hence it is not likely that a chilblain circulation is concerned in their development. The previous lesions had undergone rapid involution following roentgen therapy as an acute inflammatory process might do, which is another point against erythema induratum. I favor a diagnosis of erythema-nodosum-like inflammation with atypical features based on circulatory disturbance.

DR. CLARK W. FINNERUD: My feeling, in spite of the atypical history of the process, is that it is erythema induratum rather than erythema nodosum. It is likely that the diagnosis could be established definitely by biopsy of a specimen including the hypoderm.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: This case falls in the group to which I referred a couple of months ago and which Dr. O'Leary and I are studying in connection with members of the vascular service at the Mayo Clinic. We take a deep biopsy specimen, including one or more larger vessels in the subcutaneous tissue, and make dermal as well as cutaneous sutures. Not all of these lesions are tuberculous, and many patients are benefited by the use of a 50 per cent Pará rubber bandage.

DR. J. H. MITCHELL: The acute exacerbation since yesterday shows that the disease is probably not erythema induratum. It may have been noted that there is a considerable difference in the circulation and a 50 per cent difference in temperature of the left leg as compared with the right. The picture this patient presents today is entirely different from that of yesterday. This exacerbation suggests that the lesion probably resembles erythema nodosum rather than erythema induratum.

DR. FRANCIS W. HETREED (by invitation): The patient had many deep-seated nodules, with a good many about the ankle. The bleeding following removal of the biopsy specimen

was profuse; hence I put on a snug bandage. On removing it four days later I found that a majority of the nodules had disappeared entirely and a few that were rather large had diminished in size. I think this case fits into the group of cases of vascular disease discussed at the last meeting.

Recalcitrant Eruption of the Palms. Presented by DR. HERBERT RATTNER and DR. MAURICE DORNE.

Mrs. R. S., a white woman aged 39, has had an eruption limited to the palms for the past ten years. It appeared at the time of her only pregnancy. The eruption consists of patches of intraepidermal pustules, some superficial pustules and small brown dry flaky crusts. During the past year she has suffered from backaches, nausea and gagging. Topical treatment has failed to effect any improvement.

Examination revealed a retroverted uterus with a cervical erosion. A Graham-Cole functional test resulted in nonvisualization of the gallbladder. The basal metabolic rate was —9 per cent. The urine was normal. Examination of the peripheral blood showed a hemoglobin content of 75 per cent, 3,550,000 erythrocytes and 5,400 leukocytes. Chemical examination of the blood showed a fasting blood sugar level of 93 mg., nonprotein nitrogen 29 mg., cholesterol 161 mg. and calcium 9.9 mg. per hundred cubic centimeters.

DISCUSSION

DR. FRANCIS W. LYNCH, St. Paul: This type of case always leads to dermatologic disagreement. I think this patient has the vesicular, or moist or dyshidrosiform, type of neurodermatitis, though some dermatologists are unwilling to accept vesiculation as a feature of neurodermatitis. There is in this case a symmetric eruption of the palms without involvement of the soles, and the inflammation is relatively subacute. The patient appears to be normally concerned about the eruption, which developed in her first pregnancy, at the age of 39 years. Nervous tension is to be expected with pregnancy at that age and with the responsibility of care for the infant and the possibility of lowered estrogenic activity. The development of neurodermatitis would not be unlikely.

DR. J. H. MITCHELL: Were any bacteriologic studies of the vesicles made at any time?

DR. THEODORE CORNBLEET: This woman's hands are cold and moist. I thought it probable that she has a vasomotor disturbance. Could this be based on some focus of infection, such as Andrews had in mind as a background to his syndrome? I do not recall that vasomotor phenomena have been listed as integral parts of the so-called recalcitrant eruptions of the hands or of the pustular bacterids.

DR. FRANCIS E. SENEAR: The patient does not show a great deal of eruption today; but if the diagnosis is based on the statement in the history that there were flattened lakes of fluid or pus and the presence of brownish crusts, the conditions are characteristic of such recalcitrant eruptions. Incidentally, I may say that in his later writings Andrews has dropped the term "recalcitrant eruptions" and calls them "pustular bacterids." Basing the diagnosis on what people who had an opportunity to observe the patient have found, I am inclined to feel that the lesions in this case belong in the group of recalcitrant eruptions of the palms.

Lichen Planus with Recurrent Attacks Associated with Exacerbations of Hyperthyroidism. Presented by DR. MICHAEL H. EBERT and (by invitation) DR. M. OTSUKA.

C. T., a white woman aged 22, was first seen in the dermatologic clinic at Cook County Hospital in February 1942, with typical lichen planus. She was treated with injections of bismuth subsalicylate for three months, with no relief; so she discontinued all therapy. In February 1940 a thyroidectomy was performed for hyperthyroidism. The lichen planus disappeared within one month after operation with no local or internal treatment for it.

In August 1940 she was seen in the dermatologic clinic, with a recurrence of lichen planus on the legs. She was admitted to the medical ward for recurrent hyperthyroidism and submitted to a second thyroidectomy, in October 1940. The lichen planus disappeared again without other therapy within three weeks after operation.

In October 1942 lichen planus lesions recurred on the ankles. Her basal metabolic rate was found to be high. She was admitted to the surgical ward and given strong solution of iodine U. S. P. (Lugol's solution) to prepare for operation. The first biopsy was performed on Feb. 13, 1943; another was performed three days after the operation, and the rest of the lesion was removed. Results of a chemical examination of the blood, a blood count and a roentgenogram of the chest were normal.

The usual histologic changes of lichen planus were present: hyperkeratosis, hypergranulosis, acanthosis with a poor line of distinction between the epidermis and the cutis and a well defined cellular infiltrate in the corium.

Recurrent Lichen Planus. Presented by DR. DAVID V. OMENS and (by invitation) DR. HAROLD D. OMENS.

J. Z., a Polish steelworker aged 46, was seen on Dec. 15, 1942, at which time he presented an acute generalized inflammatory eruption with involvement of the mucous membranes of the mouth and tongue and the vermilion border of the lips which was diagnosed as acute generalized lichen planus. With treatment the eruption has subsided, with the classic changes of color. On Feb. 10, 1943, while still under treatment, he presented an acute exacerbation; this time it occurred in the classic locations for lichen planus. The patient has been at home and cannot account for the recurrence of the eruption.

DISCUSSION

DR. L. F. WEBER: I should like to ask if it is necessary to treat lichen planus with injections of drugs. I have always been impressed with the fact that lichen planus is a disease that recurs. The acute form disappears spontaneously and for the most part does well with local applications. Chronic lichen planus is often stubborn and resists all types of therapy, even injections of drugs.

DR. S. W. BECKER: I think, as I have said many times, that lichen planus is a functional disease, and hyperthyroidism always increases function and produces a recurrence. The section in the first case showed typical lichen planus. I think the disease recurs because it is difficult to keep close supervision over the patients. I cannot agree that therapy does not help, because I had a patient a couple of years ago whom I was treating with arsenic (asiatic) pills, with no improvement; in desperation I changed to use of a preparation of bismuth, and in a week the eruption was practically gone. Sometimes arsenic will help, sometimes bismuth, sometimes mercury; but treatment definitely is indicated.

DR. RUBEN NOMLAND, Iowa City: I should like to add one other treatment, administration of acetarsone. Acetarsone is popular in the treatment of pemphigus. It is equally efficacious in the treatment of lichen planus. Given in doses of 8 tablets for four days followed by three days of rest, continued for six weeks, it produces a high percentage of cures. When other methods of treating lichen planus have been exhausted, acetarsone might be tried. It is a convenient ambulatory treatment, because the patient can be given the material to take. Acetarsone is a toxic drug and probably should not be used indiscriminately in the treatment of lichen planus.

DR. OLIVER S. ORMSBY: I am sure that the treatment of lichen planus is efficacious. Recurrences do not alter this fact. I use intramuscular injections of mercury bichloride in the dose of 25 minims (1.54 cc.) of a 1 per cent solution in isotonic solution of sodium chloride. From eight to twenty injections are usually sufficient. The injections are repeated two or three times weekly. The itching usually subsides at about the fourth injection. I have cleared up recurrences three times in 1 patient, whose recurrences appeared at ten year intervals. At the time I began this form of treatment, I was using mercury biniodide by mouth, which method is much less valuable.

DR. MAURICE OPPENHEIM (by invitation): I agree with Dr. Ormsby and Dr. Nomland that heavy metals can be used in the treatment of lichen planus. I think there is a difference in the treatment of the chronic and of the acute form. The acute form yields to sodium cacodylate. I usually give 0.2 Gm. every other day or sometimes every day up to twenty-five injections. When mercury salicylarsenate was introduced, I saw good results from its use. In treatment of the chronic form I have not had such good result with the injection therapy. It is much better to give pills or drops of arsenicals. I agree with Dr. Nomland that acetarsone is valuable. If it is controlled, there is nothing to fear. In many cases asiatic pills and solution of potassium arsenite give good results.

DR. L. F. WEBER: I do not believe that this discussion has solved the problem of therapy as it pertains to chronic lichen planus.

DR. DAVID V. OMENS: I agree with Dr. Ormsby and Dr. Oppenheim with regard to treatment. Lichen planus seems to be prevalent in the Jewish race, and because of that I have had considerable experience with treatment of various types. I am convinced that neither mercury salicylarsenate nor mercury bichloride is of value in the treatment of lichen planus, but recently I have been using colloidal mercury sulfide and can say that this product has given better results in the treatment of lichen planus than any other.

DR. M. H. EBERT: I agree with those who have stated that there is a distinct value in the proper treatment of lichen planus. Treatment of the acute variety is different from that of the chronic form. It is hard for me to conceive of such definite pathologic changes being psychomatic in origin. The disease must have a more definite cause. The exacerbations and remissions which are incident to changes in hyperthyroidism suggest to me that the autonomic or sympathetic nervous system may have something to do with the disease. It is one of the manifestations of hyperthyroidism. I realize that this concept is vague, but there is still a long way to go before the cause of such a simple disease as lichen planus can be explained.

A Case for Diagnosis (Foreign Body Reaction?). Presented by DR. F. E. SENEAR and (by invitation) DR. IRENE NEUHAUSER.

A. S., a white woman aged 27, was first seen on Aug. 11, 1942, with lesions on the left thigh of six weeks' duration. The eruption had started as a single elevated purplish red tender nodule about the size of a pea which became soft and broke down, discharging thick greenish pus. Later new lesions formed, some of which enlarged without breaking down. There is no history of trauma or hypodermic injections.

On the patient's admission to the dispensary there were several flattened, boggy, deep-seated, purplish red plaques on the anterior surface of the left thigh. Two of the plaques had central sinus openings leading deep into the subcutaneous tissue and discharging purulent material. There were several hypertrophic scars present at the site of healed lesions.

Treatment consisted of local application of 10 per cent sulfathiazole ointment and administration of potassium iodide by mouth. There has been gradual healing of most of the lesions, although there are still several indurated plaques present and a small nodule has recently become fluctuant.

The Wassermann and Kahn reactions of the blood were negative. On her admission to the dispensary, the hemoglobin content was 50 per cent and the erythrocytes numbered 2,100,000 per cubic millimeter. Attempts to culture fungi from the lesions have been unsuccessful, but staphylococci have been cultured. A biopsy specimen from the front of the thigh showed the epidermis and upper part of the corium to be within normal limits except for hypertrophy of the muscle bundles about the hair follicle. The chief pathologic changes lay in the deeper part of the corium, extending to the lower limits of the section, which did not include much of the hypoderm. In this layer there were many rounded nests of histiocytic cells which were permeated by small round clear spaces. These clear spaces gave the impression of being lipoid, but they were not stained by sudan III or scarlet red and they showed no double refraction on polariscopic examination. The largest of these clear spaces were lined by flattened nucleated cells, which suggested the possibility of their being lymph vessels. In the intervening deep part of the corium there was a thickening of the walls of some of the blood vessels, and about these there was a narrow mantle of densely packed lymphocytic infiltrate. In the deepest part of the corium the cellular infiltration was more diffuse. Elastic fibers were few and fragmented throughout the corium. No acid-fast bacilli could be demonstrated by the Ziehl-Neelsen stain. No blastomycetes or other fungi were seen.

DISCUSSION

DR. HAMILTON MONTGOMERY, Rochester, Minn.: The histologic changes suggest a foreign body reaction or a paraffinoma. The clinical appearance of the lesions would also fit in with this concept. I have seen similar pituitary lesions occur at the site of injection of insulin or solution of posterior or of other hypodermic injections. Histologically, it was difficult to decide whether the cheeselike holes were spaces where foreign substances had been or whether they were newly formed vessels. It seemed to me that most of the holes were artefacts and not vessels. There were no foreign body giant cells, which one would usually expect to find if the lesions were of the nature of a paraffinoma. I could obtain no history of special treatment or injections.

DR. THEODORE CORNBLEET: The lesion on the thigh was indurated throughout, not only on the side where the nodes were but even where there appeared to be no lesions. Recently I studied tissue from paraffinomas by means of the fluorescence microscope. I found that the spaces which appear clear and empty by ordinary methods impart a turquoise blue fluorescence when exposed to ultraviolet rays. Fluorescence methods might possibly give some additional information about this woman's lesions.

NOTE.—A frozen section was not available. Sections prepared by the paraffin method showed nothing noteworthy.

DR. M. R. CARO: Staining of sections from these lesions with sudan III and scarlet red did not show the presence of fats. Examination under a polariscopic microscope failed to

show any doubly refracting particles. We shall be glad to follow Dr. Cornbleet's suggestion. (Subsequent examination by fluorescent microscopy failed to reveal fats.) I have the feeling that a much deeper biopsy specimen will have to be obtained and examined before the origin of these lesions can be determined. Most of the pathologic changes that I saw here were present deep in the corium, becoming more pronounced toward the lower limits of the section. If tissue is removed so as to include much of the hypoderm, an underlying panniculitis may be found to be responsible for the cutaneous changes.

DR. F. E. SENEAR: We thought clinically of a foreign body reaction from some injected material, but, like Dr. Montgomery, we could obtain no history to support this. We also thought of folliculitis. When the patient first was seen, the lesions were pustular in several places and had broken down. There were no such lesions present today. I question whether the disease began as a folliculitis, for, as Dr. Cornbleet said, in different places on the thigh there were deeply outlined plaques as early lesions. Some of these plaques showed an inflammatory reaction, while others could be palpated with no change in the overlying skin.

Parkes Weber Syndrome: Hemangiectatic Hypertrophy. Presented by DR. M. H. EBERT and (by invitation) DR. A. H. SLEPYAN.

B. M. T., a Negro girl aged 9 years, presents a decided hypertrophy of the right foot. Her mother states that shortly after her birth the toes of the foot were redder than normal. By the time she was 4 years of age the foot was larger than the other, and in the last three years the skin has become roughened. Trauma causes bleeding that is difficult to stop. No other member of the family is similarly affected.

At present the right foot is about one-third larger than the left. The toes are unusually wide. The tissues of the foot feel soft and spongy. The foot is definitely warmer than the left. The dorsum of the foot and the entire ankle are hyperpigmented and verruciform. On the lateral surface of the foot the verrucous surface is thrown into deep folds. There is a keloid on the ankle at the site of a former removal of tissue for biopsy. There is a mottled purplish discoloration of the sole in the region of the arch. When the child stands erect, several large varicose veins stand out on the leg and thigh. The roentgenogram showed the bones of the right foot to be larger than the left, the metatarsals particularly being considerably larger than those on the left. There are no other osseous changes.

DISCUSSION

DR. RUBEN NOMLAND, Iowa City: Wherever there is extensive enlargement, that is, hemangioma with hypertrophy of an extremity, one must think of the possibility that there is going to be a great deal of blood short-circuited between the arteries and the veins.

I should also like to mention that not only does one encounter giantism of an extremity from this cause but there can be giantism of the ears, lips and sides of the face and probably of other organs which might be affected.

DR. F. E. SENEAR: Several years ago I presented a boy who was older than this patient. He had a great deal of demonstrable enlargement of the arteries and veins and considerable enlargement of the extremity. Both of these patients presented some changes in the skin as well as vascular changes and overgrowth of the body structure.

DR. S. W. BECKER: I looked at these roentgenograms, and I do not believe there is an overgrowth of the bony structure; in fact, the bones on the affected side are atrophic. I asked the girl whether she walked on this foot as much as on the other, and she said that she did. I thought there might be a disuse atrophy, because it seemed that the metatarsal bones were atrophic on the affected side.

DR. M. H. EBERT: It was my opinion that in the roentgenogram the metatarsals were considerably longer on the affected side, but I agree that they were, if anything, more spongy. In spite of the fact that she says she uses the foot as much as the other, she limps on that side.

A Case for Diagnosis (Lichen Striatus?). Presented by DR. DAVID V. OMENS and (by invitation) DR. HAROLD D. OMENS and DR. ERHARD LOEWINSOHN.

J. M., a Negro girl aged 1 year, presents an eruption of six months' duration in the form of a line on the medial and posterior aspects of the right leg extending from just below the buttock to and involving the plantar surface of the foot and the second toe. The line starts as an almost imperceptible streak on the upper portion of the leg, and as it extends lower scaling is visible. Lower in its course the lesion assumes the form of verrucous excrescences which are easily removed, revealing a superficial involvement of the underlying areas.

DISCUSSION

DR. C. W. FINNERUD: I thought the eruption was ichthyosis hystrix, which is commonly linear and often covers the greater part of an extremity.

DR. F. E. SENEAR: I should say that this eruption did not conform at all to lichen striatus, because the lesions were so definitely hyperkeratotic, but that it conformed to the clinical picture of naevus unius lateris or of ichthyosis hystrix. I think under the microscope more change will be found than is present in lichen striatus. I did not note that this eruption went completely to the thigh, but the patients with lichen striatus whom I have seen almost invariably had a great deal more involvement of the upper portion of the extremity than of the lower; the reverse seemed to be true in this case. Also the patients whom I saw all had involvement of the upper extremity, but there is no reason why lichen striatus may not affect the lower extremity.

DR. DAVID V. OMENS: When the patient was first seen, the lesion, which is linear, was faint at the buttocks and as it extended downward on the median aspect of the thigh it became more sharply defined. The extension downward seemed to bring the lesions out to the point where they became verrucous or presented excrescences which on removal showed only superficial involvement. Permission for biopsy was refused.

A Case for Diagnosis (Herpes Zoster?). Presented by DR. M. H. EBERT.

G. F., a white man aged 58, states that two days after New Year's Day he thought he had a left-sided appendicitis, but three days later a painful urticaria-like lesion appeared on the left lower quadrant of the abdomen. He states that there had not been any trauma to the back, recent illness or focus of infection before the onset of the present trouble. He says that he had backache of thirty-nine years' duration, which was moderately improved after removal of his teeth.

When first seen three weeks ago (three weeks after the onset of the lesions) there were split pea–sized to half-dollar–sized painful urticaria-like bright red lesions along the left eleventh dorsal nerve trunk. No vesicles could be made out in any of the lesions. The patient was kept under observation, and it was only one and one-half weeks ago that vesicles developed in the lesions.

On physical examination no foci of infection could be found and no deformity was detectable in the back or spine.

Examination of the blood and urine showed normal conditions. The Kahn and Wassermann reactions were negative. A roentgenogram of the heart and lungs was normal. Roentgenogram of the thoracic and lumbar portions of the spine showed hypertrophic changes, with marginal lipping and osteophyte formation in the lower thoracic and lumbar vertebrae.

DISCUSSION

DR. HARRY R. FOERSTER, Milwaukee: Was this the case in which you stated there were urticarial wheals?

DR. M. H. EBERT: There were lesions which I should say resembled urticaria. They were raised, edematous and somewhat red but were not true urticaria.

DR. HARRY R. FOERSTER: I have seen herpes zoster show itself at the onset with edematous wheal-like elevations before vesiculation appeared, and I believe that abortive zoster in which vesicles do not develop is not uncommon. The history of localized pain with onset of the eruption and the unilateral character and grouping of the lesions favor herpes zoster, though the appearance of new lesions during an interval of approximately three weeks is confusing. I did not see the histologic section.

DR. OLIVER S. ORMSBY: Did the patient have any arsenic?

DR. M. H. EBERT: None that I know of.

DR. S. W. BECKER: When I was examining the area for hypesthesia I noted an area 10 to 15 cm. in diameter which included all the lesions, old and new. The patient may have an exceedingly wide involvement, though I think herpes zoster always appears in crops. I do not know what diagnosis should be made.

DR. F. W. LYNCH, St. Paul: After examination of this patient Dr. Laymon and I discussed the fact that leukemia and possibly Hodgkin's disease occasionally lead to the development of specific infiltrative lesions in the scars which follow herpes zoster. In Dr. Ebert's patient the microscopic appearance suggests the possibility of leukaemia cutis, though there is more evidence of perifollicular involvement than is common in that disease.

DR. S. ROTHMAN (by invitation): It seems to me that the picture is rather typical of healing herpes zoster with central necrosis. Appearance of new groups of lesions in the third week after onset may occur in this form of zoster.

DR. M. H. EBERT: I have been interested in the histologic picture of herpes zoster for a number of years; I have studied a large number of lesions at all stages of development, but I do not recall seeing anything like this.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: My thoughts concur with those just expressed by Dr. Lynch. The section showed a decided leukocytic infiltrate. I have encountered a good many cases in which herpes zoster was associated with a malignant pelvic neoplasm in the region as well as others in which it was associated with Hodgkin's disease without any specific lymphoblastomatous change in the skin. Barney has reported specific lymphoblastomatous changes in herpes zoster with lymphoblastoma. Lesions of herpes zoster sometimes persist and new lesions form over a period of months. The epidermal changes in the sections presented were minimal and not suggestive of zoster.

DR. M. H. EBERT: I took into consideration the possibilities that have been mentioned (cancer, arsenic and lymphoblastoma) as being contributory to the itching herpes zoster. The roentgenogram of the spine and back showed no visible evidence of infiltration. That does not rule it out. As for the lesions themselves, however, the most convincing thing, as I have said, was the histopathologic picture. Dr. Otsuka and I performed two biopsies, one three weeks ago, when the lesions looked like early zoster though the patient gave a history of their being present for three weeks, and another one week ago, when the lesions were hemorrhagic and presented the typical changes of herpes zoster. It may be that we missed the exact site and did not get the exact place for removal of the specimens, but Dr. Otsuka has had a great deal of experience in selecting the right place for a section. In the first section I looked carefully in the epidermis, in the blood vessels and in the connective tissue for nuclear inclusions, which are usually present at that stage of herpes zoster, but I found none. I have had no opportunity for a similar study on the later section.

A Case for Diagnosis (Lichen Planus?). Presented by DR. THEODORE CORNBLEET and (by invitation) DR. DAVID COHEN.

R. T., a white man aged 41, employed as a machinist, presents an eruption on the left foot which began three years ago as small blisters. The initial lesions are papules, which are sharply defined and covered by scales. Some of the latter are hyperkeratotic. There is a sclerotic scar on the anterior surface of the ankle, which is smooth and shiny and measures 2½ by ½ inches (6.4 by 1.3 cm.). There is a ring of flat lichenoid pale red papules bordering this. The banded lesion can be pinched up only with difficulty. Itching is present in the lesion. On the right and left buccal mucous membranes are coin-sized depressed areas, without subjective symptoms.

Roentgen and radium irradiation and local therapy have been used. There was a reaction with swelling after the use of radium.

DISCUSSION

DR. EDWARD A. OLIVER: I can easily explain the linear scar. This man was a patient of mine. When he was first sent to me, there was a bulbous lesion on the dorsal aspect of the ankle, the result of radium therapy. I treated this radium dermatitis until it subsided, thinking that the original lesion was probably one of lichen simplex chronicus. Today the patient shows several new lesions, and these, I believe, are those of lichen planus.

DR. D. V. OMENS: I was the first to see this patient, two or three years ago. At that time he presented a single lesion about the size of a dime. It was globular with a verrucous surface. I gave him one or more roentgen ray treatments. He complained bitterly that he was not getting well. I sent him to Dr. W. L. Brown for radium treatment.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: The histologic changes were typical for lichen planus.

DR. MAURICE OPPENHEIM (by invitation): The impression I got today was that this was a case of lichen striatus and belonged to the group of lichen planus. The lesions in the mouth are not characteristic for lichen planus or for Fordyce's disease. There are sebaceous cysts in the mucous membrane of the cheek. The presented case belongs to the group of lichen planus, variety lichen sclerosus.

DR. THEODORE CORNBLEET: While this man is employed at the present time, I wonder if he does not have in mind some medicolegal procedure. He blamed his present illness on the excessive use of radium. Certainly he does not show any evidence of a radiodermatitis.

Lupus Erythematosus Disseminatus Subacutus. Presented by DR. M. H. EBERT and (by invitation) DR. M. OTSUKA.

J. I., a white man aged 33, presents an eruption on the face, the V of the chest and the arms of two months' duration. He gives a history of arthritis of the left knee and both elbows for two years. In 1935 he received antisyphilitic treatment for one year. He says that he has not had any other illnesses and has taken no medicine recently. For six months he has worked with cutting oils, which caused an oil acne on the thighs and to a less extent on the forearms.

There are several coin-sized plaques on the face. Some are bright red and slightly raised, with exaggerated follicular openings. On others there is an adherent keratotic scale. The lesions on the upper part of the sternum and on the extensor surfaces of the forearms vary in size from that of a match head to that of a split pea and have a central keratotic scale. There are no lesions in the mouth. There is a general adenopathy. The spleen is palpable 1 fingerbreadth below the costal margin. The patient has many decayed teeth. The hemoglobin content is 82 per cent, the erythrocyte count 4,130,000 and the leukocyte count 8,300, with a normal differential count. The Kahn reaction of the blood serum was negative. Chemical examination of the blood, urinalysis, a roentgenogram of the chest and examination of the ocular fundi indicated normal conditions.

A specimen was taken for biopsy from one of the lesions on the arm and another from a lesion on the face.

The biopsy showed in the lesion on the arm considerable hyperkeratosis with lamellation of the stratum corneum and follicular plugging. The epidermis was flattened and in small areas reduced to three rows of cells. In these areas there was ballooning of the basal layer. In the reticular portion of the corium there was moderate homogenization of the collagen and in small areas destruction of the elastica. The round cell infiltrate was perivascular and most profuse in the reticular layer but extended deeper along some of the large vessels.

In the lesion from the preauricular area all the aforementioned changes were present and much more evident, with the exception of the infiltrate, which was moderate.

DISCUSSION

DR. MAURICE DORNE: I first saw this patient two weeks ago, when he was sent in by one of the industrial surgeons with a diagnosis of cutting oil dermatitis. It is interesting to note that this is the second patient with lupus erythematosus I have seen that has been sent in as having cutting oil dermatitis. The first was a young woman of 19 who came in with acute disseminated lupus erythematosus with dermatomyositis. I urged her to go to the hospital, but her family refused permission. She died five days later. When I saw this patient, I was worried. Dr. Oliver saw him a few days later and confirmed the diagnosis, and I was able finally to get him into the hospital.

DR. EDWARD A. OLIVER: I saw this man a week ago. It was interesting to me that he then attributed his trouble to cutting oil. I wonder how many cases of cutting oil dermatitis reported are actually cases of that disease. The patient shows typical subacute disseminated lupus erythematosus.

DR. M. H. EBERT: Through the courtesy of Dr. Dorne and Dr. Oliver we are able to report this case. There are some interesting features. One is the simultaneous appearance of the discoid type of eruption on the face and the disseminated type on the arms and V of the chest, correspondingly different in histologic structure. The most interesting feature was the general adenopathy, which is present in most patients with acute disseminated lupus erythematosus and which is rarely seen in the subacute type. The man shows no systemic disturbances as yet. The association with cutting oil is interesting but incidental. Other cases of the same type should be watched for.

A Case for Diagnosis (Superficial Nonulcerative Syphilis?). Presented by LIEUTENANT COMMANDER WILLIAM K. FORD, MC-V(S), U.S.N.R. and (by invitation) LIEUTENANT EUGENE A. HAND, MC-V(S), U.S.N.R.

J. C., a youth aged 19, has had an apruritic eruption for over two years. It began on the arms and spread slowly over the trunk, legs and arms. There has been no treatment of any kind. Several days ago he had a premarital blood test, which was reported as eliciting a 3 plus reaction. When the test was repeated, the Kahn reaction was 4 plus.

The patient admits intercourse with two women over a period of two years. He states that the eruption was present before he first started his sexual experience. There is no history of interstitial keratitis or other stigmas in the family so far as he knows.

He presents a scaly erythematous type of eruption on the trunk, arms and legs. In addition, on the legs and arms there are numerous serpiginous lesions with central normal areas. This border is dully erythematous. The eruption is superficial, with little induration and little scaling.

Since his first examination the patient has had intravenous injections of mapharsen in doses of 0.09 Gm. and intramuscular injections of bismuth subsalicylate in doses of 2 grains (0.13 Gm.).

A Case for Diagnosis (Scabies? Syphilis?). Presented by LIEUTENANT COMMANDER WILLIAM K. FORD, MC-V(S), U.S.N.R. and (by invitation) LIEUTENANT EUGENE A. HAND, MC-V(S), U. S. N. R.

J. K., a Negro aged 31, presents a sore throat, a pruritic eruption and a lesion on the toe. Six months ago he had sexual intercourse, which was followed in one month by a penile sore which disappeared after two weeks without medical care. Two or three weeks ago he began to have a sore throat, which has persisted. About the same time a soft corn between the fourth and fifth left toes, which he had had for years, began to spread and become moist. For about a month he has had an itchy eruption. He had no treatment before admission to the hospital.

On the hands, arms, trunk, legs, buttocks, genitals and inner surface of the thighs there is a papulopustular and papulovesicular eruption. There are numerous excoriations and a few typical burrows.

On the inner surface of the cheek and on the soft palate, spreading over the anterior pharyngeal fold, there is a superficial eroded lesion. The base is acutely erythematous. Over portions of these patches there is a whitish membrane.

Between the fourth and fifth left toes there is a moist sodden lesion with an erythematous base. At the upper border of this lesion is a fissured papule. (Spirochetes were encountered in dark field examination of tissue from this point.)

The Kahn reaction was 4 plus.

Since admission the patient has been given intravenous injections of mapharsen, 0.09 Gm. per dose, and intramuscular injections of bismuth subsalicylate, 2 grains (0.13 Gm.) per dose.

DISCUSSION ON CASES OF LIEUTENANT COMMANDER FORD AND LIEUTENANT HAND

DR. C. W. LAYMON, Minneapolis: I agree with the diagnoses in both cases.

DR. S. ROTHMAN (by invitation): I think that the annular lesion on the left arm has all the clinical characteristics of a late secondary lesion. However, I could not see any specific lesions on the thighs but asteatosis with cracking of the horny layer and secondary inflammatory irritation.

LIEUTENANT COMMANDER WILLIAM K. FORD, MC-V(S), U.S.N.R.: In the first patient, we felt that the atrophy was a thin atrophic scarring with an acriform arrangement on the thighs and a somewhat suggestive appearance on the legs. The scaling and irritation about it were not present yesterday. I think Dr. Hand's interpretation, that it is purely an irritation from clothing, is correct. The other case speaks for itself.

A Case for Diagnosis (Subsequently Proved to Be One of Syphilis). Presented by DR. CLARK W. FINNERUD.

E. W. R., a man aged 33, was first seen today because of a generalized eruption of about five months' duration. There were few or no subjective symptoms. One month previous to the appearance of the eruption, the glands of the left side of the neck became swollen. These swellings were preceded by headaches for three weeks and a loss of 15 pounds (6.8 Kg.) in weight. His local physician gave him a sulfonamide compound by mouth, and one week later redness and scaling were noticed on each palm. The lesions had spread rather steadily over the trunk and extremities, the principal areas of involvement being the hands, wrists and forearms. New lesions were said to begin as pinhead-sized pustules, which dried to match head-sized or larger papules.

Examination reveals a generalized somewhat violaceous papular eruption, the papules in places discrete and in other areas grouped into plaques. Many of the papules present a desiccated follicular pustule in their center. One somewhat indistinct finger nail–sized circinate papule is present on the mucous membrane of the lower lip. Hyperpigmentation is present at the site of the lesions which have undergone involution. There is general adenopathy.

The leukocyte count was 10,950. Microscopic sections from the cervical and inguinal lymph glands were compatible with the diagnosis of round cell lymphosarcoma.

DISCUSSION

DR. C. W. LAYMON, Minneapolis: To me this is one of the most interesting cases of the day. Although I could not make a definite diagnosis, I thought of two possibilities: lymphoblastoma and sarcoid. Dr. Montgomery thought that the histologic picture of the node was that of lymphosarcoma. I hope that Dr. Finnerud can perform a biopsy on one of the cutaneous lesions.

DR. M. J. REUTER, Milwaukee: There was a history of the patient's having taken sulfathiazole. I should like to suggest that as a possible explanation for the pustular eruption. I have seen several pustular eruptions due to sulfathiazole.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: The histologic changes in the lymph node were consistent with those of a small round cell lymphosarcoma, with no evidence of Sternberg or Dorothy Reed giant cells as seen in Hodgkin's disease. The clinical picture was unique, especially in view of the history that the lesions had all started as small pustules and had later become lichenified. I have not seen a lichenified pustular eruption in association with lymphosarcoma, but I have seen such a change in association with leukemia.

DR. C. W. FINNERUD: I had considered the diseases that have been mentioned, especially tuberculid, drug eruption and a nonspecific type of toxic eruption from a lymphoblastomatous process, as well as the possibility if not the likelihood of its being a rare cutaneous manifestation of what apparently the patient has in the lymph glands, a lymphosarcoma. Immediately before the eruption began on the hands, the man received one week's therapy with one of the sulfonamide compounds. About the only other thing that is not mentioned in the history is the fact that the Wassermann and Kahn reactions of his blood were negative.

ADDENDUM.—The histologic sections were strongly suggestive of syphilis. A provocative injection was given, and fourteen days later the Wassermann and all flocculation tests gave 100 per cent positive results. During this period the cutaneous lesions almost entirely disappeared, except for pigmented relics. It was considered likely that the glandular as well as the cutaneous manifestations were those of syphilis.

A Case for Diagnosis (Colloid Milium?). Presented by DR. E. A. OLIVER and (by invitation) DR. S. M. BLUEFARB.

L. B., a man aged 47, stated that as far as he can remember "little tumors" have been present on his face since the age of 6 years. There has been an increase in the number of the lesions in the past several years. There are no subjective symptoms.

On the face and neck there are several hundred pinhead-sized to pea-sized white to yellow discrete solid elevated lesions.

DISCUSSION

DR. C. W. LAYMON, Minneapolis: I thought that this was a most unusual case. I did not think that the disease was naevus sebaceus of Jadassohn, which on histologic examination shows an abundance of sebaceous glands, which were not present in these lesions. A diagnosis of syringoma or benign cystic epithelioma does not fit in this case. Another possibility is colloid milium, although this usually occurs in older persons. The conditions observed on histologic examination, however, are consistent with such a diagnosis.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: I thought this was probably a case of colloid milium, but it is difficult to make a diagnosis merely on a section stained with hematoxylin and eosin. There is a diffuse degeneration of the connective tissue, which stains blue with hematoxylin. It is true that there is some immaturity of the sebaceous glands, but these do not seem to be increased in number sufficiently to warrant a diagnosis of a sebaceous adenoma.

DR. S. W. BECKER: I was impressed with the fact that many of these tumors showed a core in the center such as is encountered in the benign type of adenoma sebaceum. The section showed a sebaceous gland and colloid degeneration. This man is 47 years old; the lesions could be degeneration and atrophy of colloid material. I reviewed the literature in connection with a paper Dr. Reuter and I wrote on colloid degenerations, and I do not believe that colloid milium as extensive as this occurring at the age of 6 years has ever been reported. If it is colloid milium, it is most unusual. The degenerated colloid material was not located in masses, as is usually described in colloid milium. I am of the opinion that acquired adenoma sebaceum does not occur before puberty, but it is not inconceivable that it could do so.

DR. EDWARD A. OLIVER: I questioned the man carefully, and he told me that he does not remember the time when he did not have the eruption. The long duration is what has made it a troublesome problem for us.

A Case for Diagnosis (Moniliasis?). Presented by DR. DAVID V. OMENS and (by invitation) DR. HAROLD D. OMENS and DR. ERHARD LOEWINSOHN.

B. D., an American girl aged 3½ years, was admitted to the Cook County Children's Hospital on March 17, 1942, because of an eruption involving the mucous membranes of the mouth, tongue, lips, nose, scalp, neck, hands and genitalia. The eruption in the mouth consisted of loosened epithelium with superficial erosions; the lips were inflamed, and there were exudates and crusts. On the ears, neck, scalp and genitalia there were vesicopustules with crusts and weeping and necrotic excavations.

On April 29, 1942 the patient was seen by Dr. D. V. Omens, who made a diagnosis of moniliasis with secondary pyogenic infection, which was confirmed by cultures in the bacteriologic department of the hospital. The patient was subsequently seen by several attending physicians, who offered various suggestions as to therapy. To date the disease has resisted all forms of treatment.

Repeated laboratory examinations have given results that varied only slightly. The latest data are as follows: hemoglobin content, 66 per cent; erythrocytes, 3,300,000; leukocytes, 7,800, with 62 per cent polymorphonuclears, 19 per cent eosinophils, 11 per cent lymphocytes and 8 per cent monocytes. Culture of material from the mouth revealed a heavy growth of monilia; culture of material from the scalp yielded Staphylococcus aureus. The vitamin C level was 1.55 mg. per hundred cubic centimeters. Arsenic was not encountered. The Frei reaction was negative. Sternal puncture showed no evidence of leukemia. All urinalyses gave normal results.

Treatment has consisted of administration of cod liver oil, ascorbic acid, brewers' yeast, sulfathiazole, blood transfusions, acetarsone, fever induced by vaccine (100 million organisms given intravenously), potassium iodide and sulfathiazole, pertussis vaccine, sulfapyridine, 50,000 U. S. P. units of vitamin D, intramuscularly twice a week, 100 mg. of ascorbic acid daily, ½ ounce (15 cc.) of elixir cofron (a preparation of liver, iron and copper) twice daily, 4 cc. of vitamin B complex daily and 0.5 Gm. of sulfapyridine four times a day. Locally the patient was given sodium perborate mouth washes, 5 per cent chromic acid, to oral lesions, sulfathiazole ointment, ammoniated mercury ointment, penicillin, ultraviolet radiation, wet dressings of potassium permanganate and copper sulfate, pine tar, yeast paste and roentgen ray therapy.

DISCUSSION

DR. CLEVELAND WHITE: The case is extremely interesting. I did not see anywhere in the report that the organism isolated was Monilia albicans. Presence of yeast organisms, unless they are monilia, may not mean a great deal. The eruption is probably a much more deeply seated process than an infection with Monilia albicans.

DR. MINNIE O. PERLSTEIN: I originally saw this patient two months ago, at which time she showed a much more extensive picture than she does today. She had severe ulcerating crusting lesions involving the lips, mouth and sides of the neck and extending onto the head. At that time I made a suggestive diagnosis of dermatitis herpetiformis. She had occasionally had recurrent lesions on the trunk which had healed, leaving a hyperpigmented residue. The eruption on the face, scalp and mouth had been progressive. The hematologic picture is extremely interesting. During the year she has been in the hospital she has shown no signs of toxemia. Her general condition is good. She has had no fever, except when she had some intercurrent infection of the upper respiratory tract. Her leukocyte count is 12,000, with eosinophils varying from 19 to 59 per cent and averaging 36 per cent. She has had every sort of treatment, local and internal. Sulfapyridine was tried, but since she did not get well in three weeks its use was discontinued. Two weeks ago she looked even worse than I originally saw her, because, in addition, she had lost most of her hair as a result of exposure to roentgen rays. She was really pathetic. She was extremely irritable, crying constantly. She had a severe bilateral perlèche, with the fissures extending halfway across the cheek. She was given polyvitamin therapy parenterally, starting exactly two weeks ago today. At the same time sulfapyridine was again given. In the past two weeks the child has made miraculous improvement. Two weeks ago she had actual craters on the scalp with ulcerative crusting lesions. Within four days after the beginning of treatment with parenterally administered vitamins and sulfapyridine, the perlèche improved. The mouth has healed; the irritability has decreased, and the child plays and talks with the attendant. I think she has dermatitis herpetiformis with a superimposed vitamin B disturbance.

DR. M. H. EBERT: When I first saw this child, I was impressed with the extensive involvement of the mucosa and thought that it was a monilia or yeast infection; but we were unable to demonstrate any yeast from the skin or mucous surfaces. Painting with gentian violet gave no relief. The objection to a diagnosis of dermatitis herpetiformis is the extent of the eruption on the mucosa, which is unusual in this disease. I agree with Dr. Perlstein on therapy. She suggested high vitamin therapy parenterally and sulfapyridine and the child has improved greatly. She is far from being well.

DR. D. V. OMENS: There is no doubt the child has improved considerably since April 29, 1942. Perhaps the reason for improvement is not the medication but the amount of roentgen therapy she has received. I do not believe the mouth is any better today than when I first saw her. Personally, I feel that I have exhausted my resources for therapy. Therefore we brought her here today hoping to get some suggestions.

DR. M. H. EBERT: This child is under the direction of expert pediatricians in the Cook County Children's Hospital.

DR. THEODORE CORNBLEET: Assuming that monilia infection had something to do in the causation of this disturbance, it brings to mind what the physicians of the Mayo Clinic refer to as submucous thrush. The term is not clear to me; therefore I should like to have one of them discuss it. Martin, at a meeting of the Society for Investigative Dermatology, described a therapeutic method for dealing with systemic mycosis which he found successful. It consisted of the use of a vaccine as well as chemotherapy. His method might be of some use in treating this patient.

DR. EDWARD A. OLIVER: I should like to ask if this child has ever been given solution of potassium arsenite. If she has dermatitis herpetiformis, it will act almost as a specific, and children stand it well. I recommend it rather than sulfapyridine for treatment of this child.

DR. D. V. OMENS: She has not had solution of potassium arsenite; she had diethylstilbestrol.

DR. MINNIE O. PERLSTEIN: She had solution of potassium arsenite for one month, but with the hemoglobin content of 50 per cent I did not think it would cure her. Unless her general health was improved, nothing would help. And it apparently requires a combination of parenterally administered vitamins and sulfapyridine to effect a cure.

DR. J. H. MITCHELL: Has the question of streptococcic infection been investigated? I am interested in the presence of monilia and streptococci in perlèche. I have a series of preparations in which both Monilia and streptococci were obtained from a patient at the same time, long chain streptococci and monilia spores. If one cares to take the trouble to look for them, one will find them both in many instances. It is a question which is causing the trouble. I think it is not exactly fair to assume that because monilia are encountered in perlèche it is the causative agent. When it is not found, I see no reason for assuming that it is the causative organism. Both organisms must be looked for in perlèche.

Melanosis of Unusual Type. Presented by DR. S. W. BECKER.

M. M., a white woman aged 30, with olive complexion, first noted a large brown macule in the right inguinal region three years ago. From that time to the present, similar lesions have appeared on the abdomen, chest and neck and in the axillas. The individual lesions have deepened in color and have persisted. The surface has shown no change from the normal, and no sensation has been experienced. The only medication used at the time of onset was some form of thyroid substance. She had suffered with sunburn followed by freckles six months previously, which, however, involved the back and extremities, areas not involved by the presenting dermatosis. On exposure to sunlight, she inclines to tan rather than to burn.

Her general health has remained good. Examination in November 1942 showed no general physical abnormalities except that she was moderately overweight. Several teeth had been devitalized. The blood count and urine were normal. Her blood pressure was 120 systolic and 80 diastolic and her basal metabolic rate was —6 per cent. She was given a reduction diet at that time.

Scattered over the abdomen and lower part of the thorax, with slight involvement of the neck and axillas, are rather brown round oval and irregular plaques varying up to several centimeters in diameter. The perifollicular regions are slightly lighter. The cutaneous surface over the lesions appears to have a normal texture.

A specimen removed from a plaque on the right upper quadrant of the abdomen was prepared by both the paraffin dopa and the silver method. With the dopa technic the reaction was moderately positive in melanoblasts, some of which were somewhat dendritic. With

the silver method, the epidermis was moderately hyperpigmented. Little or no melanin was visible in dermal chromatophores, which was in accord with the brown color of the lesions.

Since the eruption is on the covered portions of the body, it is interpreted as constituting melanosis of internal origin; this, however, does not correspond with the usual varieties of hyperpigmentary dermatosis.

DISCUSSION

DR. F. W. LYNCH, Minneapolis: I thoroughly agree with the diagnosis.

DR. S. W. BECKER: The patient was seen at a meeting of a dermatologic society in Washington, D. C., and she said that the members called it hyperpigmentation and offered to give her a paste of some sort. I have no reason to know why she has it. It may fall into the group of chloasmas, which includes a great variety of disorders characterized by hyperpigmentation. A careful study of the patient revealed no abnormality.

DR. M. H. EBERT: It seems to me that this extraordinary pigmentation may be associated with some endocrine disturbance. The same endocrine disturbance that caused the obesity may have produced the hyperpigmentation.

A Case for Diagnosis (Lupus Erythematosus?). Presented by DR. HERBERT RATTNER and DR. MAURICE DORNE.

L. A., a Negro woman aged 25, has had lesions on her arms and forearms for the past eighteen months. The lesions are finger nail sized, discrete, grouped and roughly symmetric. They are atrophic, the scars nonretracted with smooth surfaces that are hyperpigmented.

The Kahn reaction of the blood was negative, and the urine was normal.

DISCUSSION

DR. M. R. CARO: The histologic changes in this case are not consistent with the diagnosis of lupus erythematosus. The islands of perivascular infiltrate suggest the possibility of syphilis, although the section is by no means diagnostic.

DR. MAURICE OPPENHEIM (by invitation): I was thinking not only of syphilis but of papulonecrotic tuberculid. The positive tuberculin reaction is significant for a papulonecrotic tuberculid. Sometimes the reactions with tuberculin are delayed.

DR. M. H. EBERT: I saw these sections some time ago, and there was a deep perivascular infiltrate. In one I thought I saw an infiltrate suggestive of tuberculid. While I could not rule out syphilis, I agree with Dr. Oppenheim that this is more probably a hematogenous type of tuberculous infection.

DR. F. W. LYNCH, St. Paul: The three diagnostic possibilities which I considered were lupus erythematosus, sarcoid and syphilis. I think the first two can be ruled out by study of the microscopic section; the third possibility, that of late nodular syphilis, would be supported by the microscopic changes, though they are by no means diagnostic. With modern serologic methods one should hesitate to diagnose syphilis in the face of negative reactions.

Pemphigus of the Mouth Improving with Acetarsone Therapy. Presented by DRS. S. J. ZAKON and MAURICE DORNE and (by invitation) DR. E. A. SKOLNIK.

S. K., a Jewish woman aged 71, began to complain about soreness in the mouth in July 1941. Examination at that time revealed areas of redness on the hard palate and gums. She is edentulous. She was advised to discontinue the use of her plates and was given tablets of brewers' yeast. She returned in December 1942, with the same complaints. Examination at that time revealed numerous discrete flaccid bullae involving the mucosa of the lips, tongue and palate. On physical examination there were hypertension (pressure 210 systolic and 100 diastolic), hypertensive retinopathy, varicose veins and ulcers. There was a trace of albumin in the urine. Examination of the blood showed 5,090,000 red cells, 85 per cent hemoglobin and 14,750 leukocytes, of which 66 per cent were segmented neutrophils, 1 per cent eosinophils, 26 per cent small lymphocytes and 7 per cent monocytes. Platelets numbered 150,000.

Therapy with acetarsone was instituted on Jan. 25, 1943, and a decided improvement has been noted.

DISCUSSION

DR. MAURICE OPPENHEIM (by invitation): If a lesion which is present in the mucous membrane does not respond to any treatment for a long period, one must suspect it to be a primary lesion of pemphigus chronicus. If pemphigus starts in the mouth, it can be expected

to be pemphigus vegetans, as my teacher, T. Neumann, the first to describe pemphigus vegetans, taught.

DR. S. J. ZAKON: We at Mount Sinai Hospital are probably a little more conscious of pemphigus than are the physicians at other places, because we have seen more than our share of it. When a patient with a bullous eruption in the mouth fails to respond to ordinary treatment, we administer acetarsone. This patient was given acetarsone on January 25. She took 12 tablets, and there was improvement. Will the improvement continue? That is to be seen.

Congenital Ichthyosiform Erythroderma. Presented (by invitation) by DR. STEPHEN ROTHMAN.

This 18 year old white man, a farmer, from the age of 3 months to 3½ years had an eruption consisting of redness and scaliness of scalp, ears, eyelids, axillas and pubes. Later he had less eruption, but his skin never became completely smooth and flesh colored. In January 1941, the eruption broke out with full force again on the calves, popliteal fossae and thighs, ankles and dorsa of the feet. Since November 1940 he has had grand mal attacks. There is no consanguinity in the parentage and no family history of cutaneous diseases or of grand mal.

On admission to the hospital, in November 1941, the scalp, face and entire body surface were erythematous and covered with lamellar and branny scales. On the thighs and legs, in addition to scaling, oozing and crusting were seen in ill defined areas.

The Wassermann and Kahn reactions were negative. The blood and urine were normal.

With treatment with bland ointment bases with and without 0.5 per cent salicylic acid, the eruption has changed abruptly from high degrees of erythema and exfoliation to an almost normal skin. However, in spite of continuance of the same treatment, there was a relapse.

Histologic examination showed a psoriasiform picture of the epidermis and lack of a hyperkeratotic layer. This section was similar to that of the first case of ichthyosiform erythroderma reported by Dr. Udo J. Wile (ARCH. DERMAT. & SYPH. **10**:487-498 [Oct.] 1924). There was a dense infiltrate in the edematous upper part of the corium.

DISCUSSION

DR. F. E. SENEAR: I think this is clearcut congenital ichthyosiform erythroderma. The thing that interested me was that in cases of generalized ichthyosiform type the patients do not necessarily have the lack of perspiration which characterizes ordinary ichthyosis. This young man said that he perspires rather profusely.

DR. S. ROTHMAN (by invitation): Clinically we diagnosed the eruption as congenital ichthyosiform erythroderma, but we became hesitant when we saw the histologic picture, which was psoriasiform with acanthosis, elongated interpapillary pegs and papillae ascending close to the surface, but without thickening of the stratum corneum. Also, we were puzzled by the absence of a history of the recessive type of inheritance and by the fact that the eruption cleared up almost completely with bland local treatment in the hospital. Soon, however, the patient relapsed, in spite of continuation of the same treatment. We found in Dr. Wile's article the same histologic picture as in the case presented, and therefore we came back to our original diagnosis.

MICHAEL H. EBERT, M.D., *President*

MARCUS R. CARO, M.D., *Secretary*

March 17, 1943

Arsenical Pigmentation and Keratoses. Presented by DR. HERBERT RATTNER and DR. MAURICE DORNE.

C. P., a white woman aged 32, was admitted to the Cook County Hospital on March 2, 1943 with lobar pneumonia. She was treated with sulfathiazole. Examination of the peripheral blood on admission revealed a leukocyte count of 12,000, with 83 per cent lymphocytes, 3,400,000 erythrocytes and a hemoglobin content of 62 per cent. On March 8, a sternal puncture revealed conditions compatible with a diagnosis of chronic lymphatic leukemia.

At the time of admission, hyperpigmentation of "rain drop" type was present on the trunk, neck, arms and thighs. In some areas there appeared to be slight fading. Hyperkeratotic patches were present on the palms and soles, and there were keratoses on the dorsal surfaces of the fingers.

From June 1938 to January 1941, the patient had taken solution of potassium arsenite, 5 drops three times a day, for multiple sclerosis. The hyperpigmentation was first noted early in 1940, at which time it was considered as sun tan. The keratoses first developed two years ago, and use of the solution of potassium arsenite was discontinued. Treatment with vitamin B and liver extract parenterally administered was instituted, and since that time the keratoses and pigmentation have begun to recede.

The Wassermann and Kahn reactions of the blood were negative. Examination of the hairs for arsenic revealed 0.334 Gm. per hundred grams of hair (up to 0.001 Gm. is considered normal). Arsenic was not recovered from the nails.

DISCUSSION

DR. UDO J. WILE, Ann Arbor, Mich.: Without regard to the diagnosis, which was self evident, I am certain that there is no relation between the amount of arsenic which a patient takes and the development of hyperpigmentation and hyperkeratoses. A great many persons have taken arsenic for far longer periods and in greater amounts without acquiring hyperpigmentation. It seems that persons of the type of this patient are predisposed to the development of hyperpigmentation or hyperkeratoses. In the past, patients were given arsenic for chlorotic anemia for years. Other patients have taken arsenic for psoriasis for years, and yet it is only an occasional one who manifests this extraordinary change in the skin.

DR. C. W. FINNERUD: I think what Dr. Wile said is correct. All dermatologists have seen children who have had far too much arsenic, according to the general consensus, for eczemas and other diseases and who showed no clinical evidence in the skin of ingestion of too much arsenic. I wonder if in older persons, who are prone to acquire hyperpigmentation and hyperkeratosis, much less arsenic may not naturally be required to produce those changes than would be required in younger persons. I further believe that one person tends to acquire hyperpigmentation as the result of ingestion of arsenic, whereas another tends toward the acquisition of hyperkeratoses.

DR. J. H. MITCHELL: I think every dermatologist has seen patients who had hyperpigmentation rather than keratoses. I recall two brothers many years ago who were taking arsenic; one manifested intense hyperpigmentation and the other hyperkeratoses. I think that one or the other but not necessarily both eruptions may develop.

DR. UDO J. WILE: The United States Department of Agriculture is extremely interested in this question, and two or three years ago an investigation was started regarding the possibility of arsenical intoxication from the use of various sprays. A number of cases of arsenosis, particularly polyneuritis, hyperpigmentation and hyperkeratosis, were gathered by investigators from the Department of Agriculture. In most of these the diseases were due to the use of sprays. The subjects were exposed to arsenic for only short periods and in relatively small doses. The Department was interested in determining whether or not the arsenic spray was a factor and compelled fruit growers to wash or treat their product before it was packed, to protect the general public.

DR. HARRY M. HEDGE: I was wondering if an infection coupled with the use of the arsenic causes the keratosis and pigmentation. This woman had pneumonia, and pigmentation developed afterward. I recall 2 patients who suffered from psoriasis, both of whom had taken solution of potassium arsenite regularly for ten or twelve years. Neither of them acquired keratosis, but in 1, as a sequela of a typhoid infection while in the southern part of the state, and in the other one, as a sequela of pneumonia, keratoses and hyperpigmentation from arsenic developed.

DR. M. H. EBERT: That could not follow in this case. The hyperpigmentation is of several years' duration, and the pneumonia is of recent occurrence.

DR. MAURICE OPPENHEIM (by invitation): In collaboration on three papers (*Biochem. Ztschr.* **271**:332, 1934; *Arch. f. Dermat. u. Syph.* **170**:488, 1934; **175**:438, 1937) a chemist, Dr. Fantl, and I examined trivalent and pentavalent organic and inorganic compounds of arsenicals with regard to the deposit of arsenicals in the skin in cutaneous diseases caused by intoxication from wall paint and wallpaper containing arsenic. We found that sodium arsenate is deposited mostly in the hairs, with very little in the skin. The same holds true for sodium cacodylate. The reverse condition was found after the use of neoarsphenamine. The different ways in which arsenic enters the organism have an

important bearing on the changes in the skin. The horny elements of the skin, hair and nails and the stratum corneum are frequently the sites of deposit. This fact could explain the arsenohyperkeratosis and the warts. Arsenic has also an affinity for pigment. This fact could explain the arsenomelanosis. But a certain predisposition must be present in every skin with arsenical changes. In Austria, in the Alps, Styria and the Tirol, the so-called arsenic eaters are found. Mountaineers and guides eat arsenic for long periods, sometimes through their whole lives, to get strength and an attractive appearance. They are used to doses which would be deadly for any one else. I never noticed hyperpigmentation or hyperkeratotic changes among these arsenic eaters. There must be present a certain predisposition, a certain arsenical compound and a certain way of entering the organism to produce the well known arsenical sequelae.

DR. THEODORE CORNBLEET: I have been interested in arsenic metabolism for several years. One phase of my studies has been concerned with patients with arsenical keratoses and pigmentation. Observations on some of the subjects cover a prolonged period. Parallel to this work are experiments made on animals. There seems to be a short-circuiting passage of arsenic from bone and perhaps liver to the blood and then a return to the original sites. After a while little seems to escape through outside excretion. Little remains in the skin. The problem has become one of dislodging the arsenic from the bone reservoir and preventing its return. Parathyroid extract is efficient until the well known antihormone forms in opposition. At present I am abandoning treatment with this substance in favor of a trial of dihydrotachysterol. If the latter is effective, it will probably lack the disadvantage of possessing only temporary potency, as does parathyroid extract. This extract produces improvement in the keratoses and pigmentation induced by arsenic but as yet not a complete cure. It is too early to forecast what the final results will be, but the results at the present time seem encouraging.

DR. HERBERT RATTNER: The discussion has brought out several points: the relative importance of intercurrent infection, of the patient's constitution and of age as causative factors in the development of arsenical hyperpigmentation and keratoses. This case would seem to lend support only to the factor of constitutionality or hypersensitiveness. The patient is relatively young. Many present today can recall the 3 very young children with arsenical keratoses presented here at the meeting of the American Academy of Dermatology. The source of the arsenic in those cases was drinking water contaminated when arsenic had been accidentally spilled into a well. In those cases, certainly family susceptibility was a more important factor than age. The hyperpigmentation in our patient developed after use of the drug for six months and the keratoses two years later. In the circumstances the role of intercurrent infection would seem to be unimportant.

Psoriasis (Resistant); Perlèche; Scrotal Tongue. Presented by DR. DAVID V. OMENS and (by invitation) DR. HAROLD D. OMENS.

M. L., an Italian woman aged 64, presents an eruption of two years' duration involving the palmar surfaces and to a lesser degree the dorsal surfaces of both hands. It is not acutely inflammatory but is infiltrated with red and flaky scales covered with fissures. There is an eruption in the axillas, and the finger nails show typical pitting and onycholysis. In addition, the patient has perlèche and a scrotal tongue.

There were no abnormal conditions observed on laboratory examination.

DISCUSSION

DR. M. H. EBERT: The case is interesting because the psoriasis developed so late in life. Undoubtedly when more is known about the cause and the clinical manifestations of psoriasis some reason will be found for the fact that plantar and palmar psoriases as well as pustular psoriasis, which every dermatologist knows is extremely recalcitrant, are so peculiarly resistant to treatment.

DR. DAVID V. OMENS: Primarily this patient was shown because of the unusual combination of cutaneous manifestations. I thought some one would bring up the question of avitaminosis. I treated her with large doses of vitamin A and D and then changed to vitamin B, without any result. It is striking how resistant this type of psoriasis is. The patient does not respond to any sort of treatment, including mild doses of roentgen rays.

Urticaria Pigmentosa; Early Syphilis (?). Presented by DR. J. H. MITCHELL and (by invitation) DR. FRANCIS W. HETREED.

M. J., a white girl aged 16, was seen at the clinic on March 3, 1943. She stated that a small "pimple" appeared on her chin three months ago. She squeezed it, and the lesion

subsequently enlarged. A week later two ulcerated lesions appeared on the lower lip. The lips became red and swollen, and the glands under the lower jaw became swollen and tender. During the Christmas holidays she had a considerable amount of fever, which was attributed to the lesions on the lip and chin. Ascorbic acid, an iodine-containing ointment and 540 grains (35 Gm.) of sulfathiazole produced no apparent change in the picture.

Since the age of 6 years she has had a generalized pigmented eruption. Scratching produces urtication of these lesions.

On her first visit there was a dime-sized red nodular lesion on the tip of the chin and a similar but smaller one just below the lower lip on the left side. The lower lip was slightly swollen, and some fissures were present. The glands in the entire cervical triangle were enlarged, discrete and tender. No other adenopathy was demonstrable at that time. The oral mucous membrane was not involved. At present there is a generalized slightly brownish pigmented eruption. The individual lesions urticate when rubbed. Two injections of a bismuth preparation resulted in considerable involution of both lesions.

The Kahn, Wassermann and Hinton reactions were positive. Examination of the blood showed a hemoglobin content of 65 per cent, 4,000,000 erythrocytes and 7,400 leukocytes, with 64 per cent lymphocytes and 46 per cent neutrophils.

DISCUSSION

DR. UDO J. WILE, Ann Arbor, Mich.: I was impressed with the lupoid character of the lesions on the lip. To be sure, the duration of this lesion is extremely short for tuberculosis unless it were rapidly hematogenous. The lesions had a peculiar yellowish color and papules that looked singularly like those of tuberculosis, which may be no more than the well known mimicry of tuberculosis and syphilis. If these two lesions were isolated ones, with no others present on the body, it would seem to me to be a usual form of syphilid. I understand that the patient has had a roentgen examination of the chest which showed a considerable degree of calcification, suggesting an old tuberculous lesion. There is a history of improvement following two injections of a bismuth preparation, which also tended to support the diagnosis of syphilis, but I cannot help remarking that this is a rather unusual form of syphilid and certainly resembles a lesion of tuberculosis.

DR. C. W. LAYMON, Minneapolis, Minn.: A few of us examined the patient early, before the typed history arrived, and she told us that she had urticaria pigmentosa. We, too, were impressed by the lupoid character of the other lesion, and, although we thought of sarcoid, none of us made a diagnosis of syphilis.

DR. M. H. EBERT: I was impressed by the resemblance to a primary lesion of tuberculosis which was undergoing involution. Each of the primary lesions of tuberculosis on the face that I have seen resembles a syphilitic chancre at first, though it is not so hard. Later, as it begins to regress, it takes on the appearance of a plaque of lupus vulgaris. The draining lymphatic glands are enlarged. In this case I was impressed by the resemblance to a primary lesion (cutaneous inoculation) of syphilis. However, when the chest, which showed an area of healed tuberculosis, was examined, this was ruled out.

DR. J. H. MITCHELL: I saw this patient in the clinic before the results of the blood tests had been received and presented her with two or three diagnoses in mind. The first one to be considered was the one suggested by Dr. Ebert. Because of the great number of glands under the chin and the fact that the lesion was not characteristic of chancre, the first consideration was a primary complex of tuberculosis. Of course, the roentgenogram of the chest was not available at that time. We then aspirated the lesion and made a careful examination for spirochetes and found none. Then when we got the results of the blood tests and the roentgenograms of the chest they left us much in doubt. We purposely withheld active treatment because we wanted to show her at this meeting. The two injections of bismuth have caused considerable involution. I think if any one took the trouble to put pressure on the lesion he saw the apply jelly color. We are still in doubt. There was no suggestion of acquired syphilis anywhere else in the patient's body; she was carefully examined for it.

Granuloma Annulare. Presented by DR. FREDERICK R. SCHMIDT.

T. H., a white girl aged 2 years, was first seen in the dermatologic clinic of Grant Hospital in December 1942. Her mother stated that spots had appeared on the fingers four months previously. The child has had frequent attacks of bronchitis. Her grandfather and uncle died of pulmonary tuberculosis. There is no familial history of diabetes. There are no subjective symptoms.

Wassermann and Kahn reactions and results of tests for mycotic infections were negative. Examination of the blood and urine showed no abnormalities. The Mantoux reaction was negative.

On the dorsa of several fingers are many violaceous slightly elevated and hard nodules. Scattered irregularly over the body and extremities are about fifteen lesions, the smallest being reddish pea-sized papules and the largest circular plaques the size of a half-dollar. The margin of the larger lesions is made up of small firm rounded papules, whereas the center is suggestive of atrophy, for the skin wrinkles easily. There is a tinge of yellow in all the larger lesions.

Histologic examination of pieces of the skin removed from the early lesions showed that the epidermis was thinned and exhibited some degree of flattening of the rete pegs. Some connective tissue showed homogenization. There was a moderate degree of dilatation of the papillary vessels with mild perivascular lymphocytic infiltration. Staining for fat gave negative results.

DISCUSSION

DR. F. W. LYNCH, St. Paul: I think that the eruption, which I believe all will accept as granuloma annulare, deserves more intensive study than has been given it, though I cannot suggest what direction should be taken. There is no good explanation for its appearance in early life, its predilection for extensor surfaces and its tendency to progress to a certain point, become stationary and finally regress without treatment. In Dr. Schmidt's case the miscroscopic features are not characteristic, though they are acceptable for the diagnosis. The diagnosis of granuloma annulare can be made even in the absence of characteristic pathologic changes if the clinical appearance is acceptable.

DR. M. H. EBERT: Unless serial sections are taken clear through the block, one is often apt to find nonspecific pathologic changes instead of those characteristic of granuloma annulare.

DR. C. W. FINNERUD: I did not see the sections. I think the age of the lesion is a factor determining whether the areas in the center of the lesion show necrosis. It may be necessary to obtain serial sections in order to find such areas.

DR. FREDERICK SCHMIDT: I showed this patient for two reasons. The first was that when I first saw her the little lesions resembled in color those of xanthoma. It is known that many observers have pointed out a possible relationship between granuloma annulare and necrobiosis lipoidica diabeticorum. Bernstein (Bernstein, J. C., ARCH. DERMAT. & SYPH. **36**:282-286 [Aug.] 1937) suggested that histologically at least there is a resemblance.

The second point brought out by Dr. Lynch is the main reason why I showed this patient, namely, the paucity of histologic changes. I took two sections, one early and one after two months' duration, and neither showed anything on which one could make a diagnosis.

Fixed Type of Toxic Erythema. Presented by DRS. J. H. MITCHELL and D. V. OMENS and (by invitation) DR. FRANCIS W. HETREED.

R. A., a white woman aged 32, first noticed an eruption six weeks ago, commencing on the lower extremities and subsequently appearing on the hands, arms and face. Three days after the onset the ankles became swollen and tender. Numbness, pain and stiffness have been noticed intermittently in the ankles, knees, hands and shoulders since that time. Malaise has been present since the onset. She took some medicine for a few days shortly after the onset, but no history of ingestion of a drug since that time can be elicited.

On the lower extremities are purplish red irregular macules which do not fade on pressure. The hands show a lighter-colored papular eruption which urticates slightly with rubbing. When there is a flare-up, the lesions return in the same sites. The face shows slight pigmentary remnants at the site of former lesions.

The Kahn and Wassermann reactions were negative. Examination of the blood showed 4,700,000 erythrocytes and 10,300 leukocytes. The temperature was 98.6 F.

DISCUSSION

DR. H. J. PARKHURST, Toledo, Ohio: In view of the history I agree with the diagnosis of erythema toxicum. The peculiar type of thickening bears some resemblance to the lichenoid type of parapsoriasis.

DR. F. W. LYNCH, Minneapolis: In spite of the superficial nature of the lesions but because of their papular nature and the absence of epidermal change, I think a diagnosis of periarteritis nodosa should be given some consideration.

DR. STEPHEN ROTHMAN (by invitation): The patient presents a history of urticarial wheals, the individual lesions persisting for about six hours and then leaving a red spot. Clinically, also, the eruption impresses me as an urticarial toxic eruption. The solid con-

sistency of the raised lesions is obviously due to edema in the upper part of the corium and not to a cellular infiltrate.

DR. HERBERT RATTNER: It has been suggested that the patient has a manifestation ot allergy, and Dr. Lynch has suggested a diagnosis of periarteritis nodosa. Recent issues of the *Bulletin of the Johns Hopkins Hospital* have contained several articles tending to support the contention that periarteritis nodosa is an allergic manifestation, capable of being elicited by numerous allergenic substances. This case would seem to lend support to that view.

DR. D. V. OMENS: I saw this patient last Thursday for the first time. She presented definite inflammatory nodules in the skin; some were hemorrhagic. Now the hemorrhagic condition has faded. Dr. Lynch's suggestion is well taken. The patient seems to have some vascular correlation which would have a bearing on the diagnosis. She states that she has not taken medicine of any kind. She reported some arthritic pains in association with acute exacerbations. That occurs often. The picture we saw last week was a mixture of nodular urticarial lesions.

A Case for Diagnosis (Rosacea-like Tuberculid in Lewandowsky?). Presented by DR. DAVID V. OMENS and (by invitation) DRS. HAROLD D. OMENS and M. OTSUKA.

T. D., an Italian woman aged 40, for one year has had a papular eruption involving the nose, cheeks and chin. There are no subjective symptoms.

The Mantoux test elicited a negative reaction at the end of twenty-four hours.

DISCUSSION

DR. C. W. LAYMON, Minneapolis: At previous meetings of the society the term "rosacea-like tuberculid" has been discussed. My own feeling is that it is not good terminology to use the name of one disease to modify that of another. In many instances of tuberculids occurring on the face the only relationship to rosacea is that both diseases may occur in the same areas. Tuberculids of the face may be designated according to the size and type of the papule, since the latter lesion is the essential one in all of the various facial tuberculids. This type of eruption may be called the micropapular tuberculid, since it is composed of tiny brownish red papules.

DR. C. W. FINNERUD: I see many such eruptions (whatever they are) that have been present about a year or two in women or men of about the age of this patient. I think they constitute a type of rosacea. They do not respond to treatment, as do most rosaceas. They are aggravated by roentgen therapy. Some of the papules, occasionally with a little stretch of the imagination, under the diascope will seem to have the characteristic color of tuberculids. I believe that most of the lesions of this type are not tuberculids. They do not respond to intravenous injections of a gold salt. They prove resistant to all forms of treatment commonly employed for rosacea. I have not performed biopsies on patients with such eruptions because of the location of the lesions. I grant that there is a rosacea-like tuberculid of Lewandowsky, but this patient does not have that disease.

DR. HERBERT RATTNER: I thought that this woman presented enough telangiectases and flushing of the central area of the face to warrant calling the eruption "rosacea-like." On diascopic pressure I could not see the apple jelly color. The disease, I think, is rosacea.

DR. J. H. MITCHELL: After testing all of the lesions, I found one on the tip of the nose that gave an apple jelly color on diascopic pressure.

DR. M. H. EBERT: I agree with Dr. Mitchell that on pressure with the diascope there was some residual brown color; however, this does not necessarily indicate tuberculosis. This color can sometimes be found in ordinary acne. I hesitate to call this a tuberculid of any type. I think it is rosacea.

DR. THEODORE CORNBLEET: Would a quantitative tuberculin test be of any value in coming to a decision in this case?

DR. D. V. OMENS: I want to apologize for presenting the case in such a slipshod manner. I saw the patient in the clinic yesterday afternoon, performed a Mantoux test and had her come back so that I could read it today. Then I thought it might be well to present her. I have not arrived at any definite diagnosis.

A Case for Diagnosis (Atrophy of the Skin? Poikiloderma?). Presented by DR. THEODORE CORNBLEET and (by invitation) DR. DAVID COHEN.

M. T., a white woman aged 69, has had an eruption for seven years. It began on several areas simultaneously and spread so that at the end of three years the entire skin, excepting

the palms and soles, was involved. There is a generalized scaling erythema interspersed with coin-sized apparently normal areas with a normal amount of pigment. The entire skin seems to be atrophic and can easily be thrown up into fine, thin folds. The scalp is covered by a thick scale, and the patient complains of a feeling of tautness. There are numerous telangiectases at various places.

The blood pressure was 200 systolic and 100 diastolic. The urine was normal. Chemical examination of the blood showed 125 mg. of sugar, 14 mg. of urea nitrogen and 30 mg. of nonprotein nitrogen per hundred cubic centimeters of blood. Examination of the blood showed no abnormal condition.

DISCUSSION

DR. RUBEN NOMLAND, Iowa City: I think this is a type of atrophy that could be called poikiloderma that is possibly secondary to an extremely mild mycosis fungoides. There are one or two areas suggestive of that disease. It seems to me that microscopic examination should determine whether a diagnosis of poikiloderma following mycosis fungoides is correct. Dr. Oliver (Oliver, E. A.: Mycosis Fungoides with Poikiloderma-like Symptoms, ARCH. DERMAT. & SYPH. **33**:267 [Feb.] 1936) reported a case of such a disease many years ago.

DR. M. H. EBERT: According to my idea of poikiloderma as it is pictured in Jacobi's atlas one sees many of the changes which are present in an old roentgen ray dermatitis, namely, spotted pigmentation, telangiectasia and atrophy. These are not present in the case today.

DR. MAURICE OPPENHEIM (by invitation): Dr. Cohen showed me the slides of this case. I found definite atrophy of the skin in the end stages and no polymorphous cells in the papillary and subpapillary layers, as are found in pseudoleukemia; there were no Sternberg cells. The absence of polymorphous cells speaks against a premycotic stage, which appears as an erythroderma. I believe that this disease is not Jacobi's poikiloderma atrophicans vasculare, because there is little or no pigmentation and there are few telangiectases. The fact that the whole body is equally involved speaks clinically against the diagnosis of dermatitis atrophicans. There are scleroderma-like lesions, sharply limited areas which are not found in poikiloderma atrophicans vasculare.

DR. FREDERICK SCHMIDT: I thought that the possibility of pityriasis rubra pilaris should be considered. Some years ago Dr. Fred Wise said that a prompt diagnosis of pityriasis rubra pilaris can be made from the islands of normal skin standing out in the involved skin. In poikiloderma the inflammation includes areas of normal skin, but it does not leave islands of normal skin, as in this patient. The absence of changes on the dorsum of the fingers is seen in the early stages of pityriasis rubra pilaris but not in the later stages, but this does not exclude that diagnosis. In a conversation with Dr. Peck some time ago, he wondered if there are not a great many patients with the pityriasis-rubra-pilaris-like syndrome who do not have the classic Devergie disease.

DR. F. W. LYNCH, St. Paul: I have no diagnosis to offer, but I should like to point out two features of this patient's eruption. The nature of the scaling and the thickening of the skin lead me to believe that the atrophy is secondary rather than primary. Against the diagnosis of lymphoblastoma is the relative lack of deep infiltration. If the disturbed keratinization is a result of inflammation in the cutis, the amount of scaling observed is out of proportion to the amount of infiltration.

The second point is that I thought this patient's tongue was redder and smoother than is usual, even at her age. One border presents an area having an atrophic or scarred appearance.

DR. THEODORE CORNBLEET: I agree with Dr. Foerster that this woman's eruption does not fit the usual picture for Devergie's disease.

As to the possibility of lymphoblastoma, apparently there are no signs of it as yet in the patient's blood. As is well known, however, this does not forecast anything.

I am impressed with the new chapter being written on cirrhosis of the liver in which it is shown that nutrition may have even a decisive role. Perhaps this newer knowledge of nutrition will help to light up the dermatologic penumbra of the idiopathic atrophies. Perhaps Dr. Lynch was hinting at something of the same sort when he referred to changes in the moucous membranes.

A Case for Diagnosis (Schönlein's Purpura? Rickettsial Infection?). Presented by DR. M. H. EBERT and (by invitation) DR. M. OTSUKA.

C. W., a white man aged 37, entered Cook County Hospital on Feb. 13, 1943, with a history of chills, fever and painful joints of two weeks' duration and an eruption of two days' duration. For the first week after admission he complained of severe headache and backache. Since

admission he has had a septic type of temperature, rising in the afternoon, subsiding to 99 F. and reaching normal in the morning. The maximum temperature has gradually subsided. Since his admission he has had four distinct episodes of chills, fever, painful joints and a purpuric eruption, especially on the extremities, but with a few lesions on the trunk. The lesions are dull red macules of the size of a small coin, which do not fade on diascopic pressure. The lesions become absorbed rapidly and leave a brown residue.

The leukocyte count has been persistently low, 6,000 on one occasion and 5,400 on another. The differential count was normal with the exception that the monocytes were slightly increased. The platelet count and the bleeding time were normal. The sedimentation rate was increased. The blood was sterile on repeated cultures. The Weil-Felix reaction was negative on two occasions. A specimen of the blood serum sent to the United States Army, Department of Virus and Rickettsial Diseases, was reported not to have agglutinated any strains of rickettsias.

Two specimens for biopsy were removed from the hemorrhagic lesions of the skin. The principal changes were in the small blood vessels of the upper part of the corium. There was a proliferation of the endothelium, with perivascular infiltrate of polymorphonuclears, leukocytes and some histiocytes. In sections fixed with Regaud's solution and stained with Giemsa stain a few endothelial cells and smooth muscle cells which contained numerous minute purple-staining bodies were found.

DISCUSSION

Dr. Elmer M. Rusten, Minneapolis: I do not disagree with the diagnosis presented. However, undulant fever should be considered because of the recurrent chills and fever and the articular pains. A variety of lesions may be produced by brucellosis. I do not believe a negative agglutination reaction for undulant fever is sufficient to rule it out. A culture of the blood should also be obtained.

Dr. Ruben Nomland, Iowa City: I believe that the diagnosis in this case is probably purpura of the Schönlein type. I have encountered only 1 case of Rocky Mountain spotted fever, but I think it is hardly possible to get a recurrent purpuric eruption in that disease. It is not always spread by the tick, but one must have the tick or some other vector to pass it on.

As to the microscopic examination, I hesitate to say that the cytoplasmic granules presented here are not inclusion bodies, but I think granules presented as inclusion bodies can be mast cells. I believe the patient has ordinary purpura and that the granules are mast cells.

Dr. Arthur C. Curtis, Ann Arbor, Mich.: If this is Rocky Mountain spotted fever, it is the first time I have ever had an opportunity to see or examine a patient with the disease. Certainly the course of this patient's disease is similar to that described for Rocky Mountain spotted fever.

I do not think that one can say, as Dr. Nomland has, that these are not inclusion bodies.

If this disease is Rocky Mountain fever, where did the patient get the infection? He has never been outside Chicago. He has been a garbage handler and sleeps in flop houses. Rats or dogs may be hosts to the vectors of rickettsial disease.

Undulant fever can produce many types of eruption, but I have never seen an eruption of this kind associated with undulant fever.

It has been said that for a positive diagnosis of undulant fever the blood should yield the organisms on culture. It is almost impossible for any one but a specially trained technician to grow the organisms of undulent fever routinely on culture. I have been impressed by my inability to isolate them from the blood of patients known to have the disease.

Dr. C. W. Finnerud: I thought the conditions were compatible with Schönlein's purpura. Mast cells vary greatly in size and shape and in size and shape of their granules. Some areas in the section were so atypical that I can see how the cells might be considered rickettsial bodies, but I presume they are all mast cells.

Dr. Herbert Rattner: Some time ago there was a patient in the Cook County Hospital for whom the diagnosis of Rocky Mountain spotted fever was established with certainty. The cutaneous picture in the case presented today is identical with that in the other case.

Dr. M. H. Ebert: Naturally we should like to prove that this man has a rickettsial infection. My experience is limited to 1 case of Rocky Mountain spotted fever, that of the patient in the Cook County Hospital a year and a half ago. The microscopic observations in the case presented today are somewhat similar to those in the other case. I realize the pitfalls in making a diagnosis of rickettsial infection from the histologic sections. Pinkerton has pointed out that the beginner should beware of making a diagnosis on the basis of sections. The intracellular bodies are difficult to distinguish from the granules in mast cells. We shall not attempt to make a positive diagnosis in this case. Clinically, it does not fit

into either one of the two types of rickettsial infection which are seen in the United States, namely, the typhus group, which includes murine typhus, frequently encountered in the southern states and spread by the rat flea, and the European type, of which the body louse is a vector. In typhus of either type there is a crisis, the temperature descending rapidly to normal. In this man there has been recurrent fever. He has been exposed to unsanitary conditions and was infested with lice and bedbugs when he arrived in the hospital. The Rocky Mountain fever group of rickettsial diseases exists not only in the western part of the United States but in the southeastern portion and is transmitted by the tick. It is a disease of summer and could not well occur in the middle of winter. The hematologic picture and the recurrent crops of hemorrhagic cutaneous lesions would fit in better with the picture of Rocky Mountain spotted fever. However, the other laboratory data are against such a diagnosis. The blood on two occasions failed to agglutinate proteus organisms of strain X19. These examinations were made by the Department of Virus and Rickettsial Diseases of the United States Army.

Kaposi's Sarcoma. Presented (by invitation) by Drs. S. Rothman and A. B. Henningsen.

This 45 year old Jewish inspector was presented before this society last spring. Since then many new lesions have developed, mainly on the extremities, which have been fairly well controlled by roentgen therapy, radium and arsenicals. One lesion on the dorsum of the right hand became ulcerated, grew with exceptional rapidity and had the clinical appearance of a real sarcoma. This lesion is being treated with a radium mold.

Two months ago a lesion developed at the anterior end of the right ventricle of the larynx. Biopsy was performed, and the histologic examination showed a structure similar to that of the cutaneous lesions. Since that time the lesion has doubled its original size.

DISCUSSION

Dr. Cleveland White: It is amazing how rapidly the tumors, especially those in the lower extremities, have developed.

Dr. M. R. Caro: I agree with the diagnosis. The only feature in this case which was entirely new to me was the presence of edema and bullous lesions on the legs of a patient with Kaposi's sarcoma.

Dr. S. W. Becker: One interesting feature is the ulcer on the back of the left hand. The lesions on the hand do not ordinarily ulcerate. Sometimes those on the leg do as a result of lymphedema and vascular obliteration. I was wondering whether this ulcer might not be due to roentgen therapy or surgical removal of the tumor.

Dr. C. W. Finnerud: In a patient with Kaposi's sarcoma, especially on the lower extremities, one occasionally observes soft reddish brown nodules which can be pushed with a finger into the skin, well below its level, and which gradually reappear in the course of a few seconds, to resume their former puffy appearance.

Dr. F. W. Lynch, St. Paul: I was particularly interested in the cystic lesions mentioned by Dr. Finnerud. Though I think they are part of the pathologic process of Kaposi's sarcoma, one would expect that the cysts would contain red blood cells and that the fluid would not be clear and serous, as it appears to be here.

Dr. Stephen Rothman (by invitation): The soft, almost cystic, consistency of the lesions on the legs is probably due to lymph stasis. In answer to Dr. Becker, the ulcer of the dorsum of the right hand developed preceding radium treatment and responded well to this treatment. (May 11: The ulcer has healed almost completely.) Because of its rapid destructive growth we thought that this lesion might represent the rare development of a true sarcoma from Kaposi's sarcoma. However, histologically it never showed the features of a true sarcoma. The lesion of the larynx was a cherry stone–sized brown globular tumor on the vocal cord which doubled its size within a week. Histologically, it displayed all the characteristics of Kaposi's sarcoma.

Glomus Tumor. Presented by Dr. Theodore Cornbleet and (by invitation) Dr. H. C. Schorr.

C. J., a Negro aged 38, has had a lesion on the left calf for twenty years. During the last five years it has become exceedingly tender. The lesion is a fairly well defined hazelnut-sized tumor raised about ¼ inch (0.5 cm.) above the surface of the skin and does not seem to me inflamed. It is extremely tender. There is no history of injury at the site of the tumor.

DISCUSSION

DR. RUBEN NOMLAND, Iowa City: I think this patient gave a typical history of glomus tumor. The microscopic section was typical of the kind of glomus tumor in which the constituents are chiefly blood vessels surrounded by endothelial cells.

DR. HERBERT RATTNER: Glomus tumors are usually readily recognized. However, I once saw a patient who had been treated in several places for painful plantar warts which on removal turned out to be glomus tumors.

DR. THEODORE CORNBLEET: There is little to add except to point out that the lesion was on the left leg near the calf. Most writers state that a glomus tumor appears about the digits, especially about the nails. In other patients exhibited here, the lesions likewise have appeared more proximally. A rather recent one had a lesion on the arm. Also of interest is the fact that although a specimen for biopsy was taken from deep in the lesion with the largest punch this did not elicit any pain. Perhaps this phenomenon follows the well known "all or none" law.

Pigmented Purpuric Lichenoid Dermatitis. Presented by DR. THEODORE CORNBLEET.

C. G., a white man aged 35, has had an eruption on the legs for nine months. It consists of fine slightly raised lichenoid reddish to orange papules tending toward group formation. The color at some sites does not fade on pressure. Here and there are a few dilated capillaries. Both legs are involved almost up to the knees. The patient has had no illness of any kind, and his diet is normal.

There was a bruise last year near the site where the first papules appeared. The patient's hands turn purple easily when chilled. His toes were once frozen, and in cold weather his feet are uncomfortable. He has taken many sun baths and used the sun lamp frequently. There has been a gain of 30 pounds (13.6 Kg.) in weight during the last year.

Histologic examination of a section from the leg showed discrete microscopic papules separated from each other by normal areas. In each papule the epidermis was flattened and was separated by a narrow band of normal corium from a densely packed cellular infiltrate about the subpapillary blood vessels. Lymphocytes predominated in this infiltrate, but there were also many histiocytes which contained much iron pigment, as demonstrated by Perles' prussian blue reaction.

DISCUSSION

DR. C. W. LAYMON, Minneapolis: This disease has always been a source of confusion to me, and I think other dermatologists have the same feeling. Sometimes one encounters pigmented purpuric patches on the legs without the presence of lichenoid lesions; this is called Schamberg's disease. When papules are present, the dermatosis is called pigmented purpuric lichenoid dermatitis. The striking feature is that in both diseases circulatory disturbances are usually present. In this case the lesions are more numerous on the leg which has the larger varices. In my opinion, in most cases Schamberg's disease and pigmented purpuric lichenoid dermatitis are forms of stasis dermatitis.

DR. M. H. EBERT: In spite of the fact that it is practically impossible to demonstrate any visible elevation of this lesion, it does fulfil the criteria for Gougerot and Blum's disease. This differs from ordinary Schamberg's disease; the lesions are more discrete and regular, more like lichen nitidus. I think it is true Gougerot and Blum's disease.

DR. M. R. CARO: I think that both clinically and histologically one can demonstrate papules in this case to a much greater extent than in Schamberg's disease. I agree with the diagnosis as presented.

DR. S. W. BECKER: Results of microscopic study are important. Here the infiltrate is more localized and deeper than in Schamberg's disease. In that disease there is usually a sensitive infiltrate hugging the epidermis. The color is due to hemosiderin. In both diseases the same typical burnt sienna and cayenne pepper colors are seen.

With regard to Dr. Laymon's statements, I do not think that stasis has anything to do with the disease. In my opinion this man has not had a great deal of stasis. Schamberg's disease and pigmented purpuric lichenoid dermatitis both occur without stasis.

DR. M. H. EBERT: I think that stasis perhaps has something to do as a predisposing factor. Schamberg's disease is more often encountered in the lower extremity than anywhere else. However, I recall several patients with Schamberg's disease who had typical lesions on the arms and back and other parts of the body; hence there is definitely another factor in the causation than simple stasis.

DR. J. H. MITCHELL: In connection with what Dr. Becker said, I saw a 10 year old boy with extensive Schamberg lesions on the legs, with no evidence of stasis whatsoever.

DR. THEODORE CORNBLEET: I first saw this man in the evening and by light transmitted from the side. When the lesions were seen that way, the papular nature of the eruption was evident. Perhaps the light as it was transmitted today was not conducive to showing that part of the eruption. It seemed apparent to me that there were lichenoid elements raised above the level of the skin. This man is an athletic director in a public high school and is in perfect health except for this eruption and does not display any swelling of the ankles or anything abnormal about his legs. I am inclined to agree with those who think that stasis is not a basic factor in this eruption. There are no enlarged veins. Stasis as a factor in Schamberg's disease does not appeal to me, because the lesions in the skin may clear up spontaneously. The effects of stasis, on the other hand, should become accentuated with time. It is true that this man received a blow on the leg where several months later the changes in the skin first appeared. Still later the opposite leg became involved. My guess is that the moderate trauma was coincidental to the event that followed.

Acanthosis Nigricans of the Juvenile Type, Mild Diabetes and Obesity. Presented (by invitation) by DR. S. ROTHMAN and DR. A. B. HENNINGSEN.

This patient was shown to this society by Drs. Becker and Obermayer in May 1941. The lesions of acanthosis nigricans, which have been present since the age of 7 on the neck, in the axillas and in the umbilical region and groins, have not progressed in the last two years. The obesity is of about the same degree as it was two years ago, although the patient is not on a diet.

Two years ago a dextrose tolerance test revealed a mild diabetic curve and alimentary glycosuria. At present the urine is sugar free. The sella turcica is normal. The intelligence is above the average. The blood pressure is 144 systolic and 88 diastolic, but with exertion the systolic pressure goes up to 220. Striae are present on the shoulders.

Tubercles of molluscum contagiosum have been present on the shoulders and chest for several months and were partly removed last week. The loose atrophic scars on the chest are claimed by the mother to have developed at the site of two spontaneously subsiding molluscum tubercles. The pedunculated fibromas of the axillas have increased in number in the last two years.

DISCUSSION

DR. ARTHUR C. CURTIS, Ann Arbor, Mich.: This case brings out how little is known about the cause of acanthosis nigricans. This patient presents also some physical conditions which should lead to another diagnosis. Certainly one diagnosis is juvenile acanthosis nigricans.

This young girl is obese; her obesity has the distribution of the pituitary habitus. She has diabetes, hypertension and numerous striae. These observations lead to a diagnosis of Cushing's syndrome. If one tries to substantiate the diagnosis of Cushing's syndrome by roentgen examination, one is often wrong; in this case the sella turcica showed nothing. The pituitary tumor, if present, is tiny and often does not cause erosion of the sella turcica.

There is now considerable discussion whether Cushing's syndrome is due primarily to a pituitary tumor or to an adrenal tumor. The patient's blood pressure was high and fluctuating, and it makes one wonder if the adrenal glands are involved by tumor tissue or are hyperplastic.

If the diagnosis is Cushing's syndrome, the prognosis is bad, for in most cases the disease leads to early death.

DR. LOUIE WINER, Minneapolis: An interesting feature was the association of verruca vulgaris with acanthotic lesions. It has been noted by several writers previously that acanthosis nigricans and verruca vulgaris are seen concomitantly in the same patient.

DR. STEPHEN ROTHMAN (by invitation): I agree with Dr. Curtis that the possibility of Cushing's syndrome must be considered because of the presence of striae, decreased tolerance for dextrose, obesity and high blood pressure on exertion. However, there is no flushing of the face and no disturbance of calcification of the bones, and the distribution of the obesity is not typical. We are searching the literature for more cases of completely developed Cushing's syndrome associated with the juvenile type of acanthosis nigricans.

Like most patients with Cushing's syndrome of the juvenile type, those of the 2 familial cases of Miescher also were obese and had "diabetes." The sister died from diabetic acidosis; the brother recovered almost completely after castration (Hellerström: *Acta dermat-venereol.* **14**:86, 1933). Two years ago our patient was presented before this society by Drs. Becker and Obermayer (ARCH. DERMAT. & SYPH. **45**:236 [Jan.] 1942). Since that time her development has been somatically and psychically normal. The disturbance of carbohydrate metabolism has not become worse. The cutaneous lesions have not changed. However, a

pathologically increased tendency to formation of striae and round, loose atrophic spots has become obvious. It is noteworthy that the father of this child died at the age of 37 from a bronchiogenic carcinoma. A similar history was given in the case of juvenile acanthosis nigricans by Brünauer (*Zentralbl. f. Haut- u. Geschlechtskr.* **37**:786, 1931).

Association of fibromata pendula and of verruciform, filiform excrescences with acanthosis nigricans are of common occurrence and are reported in almost all cases.

Pemphigus Vulgaris? Presented (by invitation) by DRS. S. ROTHMAN and A. B. HENNINGSEN.

This 47 year old housewife has been suffering from psoriasis for eight years. She was treated with roentgen rays and local applications of sulfanilamide until a diffuse scaling dermatitis appeared on the face, neck, shoulders and back.

When first seen, on Oct. 16, 1942, the differential diagnosis included exudative psoriasis, dermatitis herpetiformis and streptococcic eczema. Circinate lesions with superficially eroded edges and with tendency to serpiginous configuration were present. There was no response to mild indifferent local applications. In the last three weeks she has had solution of potassium arsenite, five to ten drops three times a day, and lipocaic.

During the past week bullae have appeared irregularly on the trunk and extremities, with a strongly positive Nikolsky sign in the neighborhood of the bullae.

Laboratory examination revealed no internal pathologic changes. In October 1942, diphtheroids, hemolytic staphylococci (Staphylococcus aureus) and hemolytic sterptococci were cultured from the lesions. Histologic examination showed mild inflammatory changes.

DISCUSSION

DR. UDO J. WILE, Ann Arbor, Mich.: This is typical dermatitis herpetiformis, or the so-called Senear-Usher syndrome. The patient is hardly ill enough to have acute pemphigus. The odor associated with the lesions, the long duration and the type of scaling were all characteristic of this rather new form of pemphigus, which is encountered more often now than formerly.

DR. MAURICE OPPENHEIM (by invitation): Some of the areas gave the impression of pemphigus foliaceus. On the chest there are loose crusts and scales such as are seen in this disease.

DR. C. W. FINNERUD: Because of the chronicity and of various characteristics of the lesions, I was impressed that this is an atypical manifestation of pemphigus erythematosus.

DR. M. H. EBERT: That was my impression.

DR. STEPHEN ROTHMAN (by invitation): I should like to ask Dr. Wile and Dr. Finnerud whether they would make a tentative diagnosis of dermatitis herpetiformis before the appearance of bullae. I do not think it is either pemphigus vulgaris or dermatitis herpetiformis.

DR. UDO J. WILE: Ordinarily the excoriation and the herpetiform character come after the bullae appear. The differentiation from dermatitis herpetiformis is in the relative absence of itching. Both diseases start as a mild form of pemphigus and become intensely exfoliative. There can be a positive Nikolsky sign without bullae.

DR. S. ROTHMAN: The patient has had intense itching and scratch marks. There is no doubt that she has psoriasis. When first seen, she had old lesions on the legs and knees typical of psoriasis.

A Case for Diagnosis (Subsequently Proved to Be One of Syphilis). Presented by DR. C. W. FINNERUD.

Last month I presented a patient as possibly having cutaneous lymphoblastoma. He came in with a diagnosis of lymphosarcoma, based on sections taken from some of the enlarged lymph glands. He was presented with that diagnosis. I stated at that time that the section from the gland was not incompatible with lymphosarcoma, in that many of the round cells showed mitotic figures. Dr. Hektoen later saw the sections and had the same impression. A section from the wrist showed what Dr. Hamilton Montgomery and I thought to be a granuloma, possibly of syphilitic origin. The question at the time of presentation of the case was whether the lesion was a specific or a nonspecific cutaneous manifestation of lymphosarcoma. The patient came in with a history of negative Wassermann and Kahn reactions. When I next saw him, I gave him a provocative injection of neoarsphenamine, two weeks after which both the Wassermann and the Kahn reaction were 100 per cent positive. The eruption is now gone, except for hyperpigmentation remaining at sites of the previous lesions. Hence I feel rather certain that the cutaneous manifestations were purely on a syphilitic basis and that it is not unlikely that that disease also accounts for the glandular manifestations.

LOS ANGELES DERMATOLOGICAL SOCIETY

L. F. X. Wilhelm, *President*

A. Fletcher Hall, *Secretary*

March 9, 1943

A Case for Diagnosis. Presented by Dr. Chris R. Halloran.

Mr. H. W., a 64 year old white man, states that a "birth mark" appeared on the lateral aspect of the right shoulder ten years ago; the lesion was flesh colored when it first appeared. Three years ago he brushed against a wall and injured the lesion. Since that time there has been a slowly growing ulcer at the site of the former "birth mark."

At present, the lateral aspect of the right shoulder presents a quarter-sized lesion, the margins of which appear atrophic. The center of the lesion is a nickel-sized area of what appears to be granulation tissue. No biopsy or other laboratory examinations have yet been made.

DISCUSSION

Dr. Saul Robinson: My diagnosis is epithelioma, probably a mixed type, both basal and squamous cell. I think therapy should be removal of the entire lesion with a cautery.

Dr. H. C. L. Lindsay: I agree with Dr. Robinson. The lesion should be removed with an electrocautery, and it should be done thoroughly. It is advisable to close the wound by plastic procedures or by a skin graft, if there is apt to be too much distortion.

Dr. N. P. Anderson: I think the most interesting point about this case is the fact that no arsenical keratoses were present on the palms but a great number were present on the soles. I think that the lesion is a so-called benign superficial epithelioma. In this particular instance it may be of a mixed type, owing to the proliferation in the center of the lesion, but I believe it is of arsenical causation.

Dr. H. C. L. Lindsay: Recently I have seen two epitheliomas, clinically definitely of the superficial type, which on microscopic examination proved to be of the prickle cell type. One cannot be certain of the type of cancer by palpation and appearances alone.

Dr. Samuel Ayres Jr.: I agree with Dr. Anderson's remarks.

Dr. Stanley Anderson: I think the lesion is an epithelioma of a mixed cell type. The original lesion had existed a long time and was probably of a superficial cicatrizing type. The more recent growth is likely due to the superimposed squamous cell lesion.

Dr. L. F. X. Wilhelm: I was in the room when Dr. Anderson looked at the patient's feet, and I also was struck by the fact that there were no keratoses on the palms while there were so many on the soles.

Note.—Biopsy showed the lesion to be an intraepidermal epithelioma, and the Wassermann reaction was negative.

Keloid. Presented by Dr. J. R. Bancroft.

A. B., a middle-aged negress, states that in 1937 a keloid was removed surgically and no after-treatment was given. Within two months of the operation for removal, the lesion began to recur, at first in the line of incision at the site of the stitch marks. It began to spread out until it now is about 2 inches (5 cm.) long and 1¼ inches (3 cm.) wide and is lobulated. It projects about ⅜ inch (1 cm.) from the surface of the skin and is roughly lobulated into three lobes on either side of the midline.

DISCUSSION

Dr. M. E. Obermayer: A few days ago a local surgeon called my attention to a mode of internal treatment for keloids, which he has been using with alleged success for several years. It consists of the peroral administration of a 1 per cent aqueous solution of sodium fluoride, 5 to 10 drops three times a day on an empty stomach. Realizing my skepticism, he showed me a clinical note in the *Münchener medizinische Wochenschrift* (**38**:1534 [Sept.] 1935) by Cadlam, in which the author claims that any keloid will disappear in from two to three months by the daily administration of about 0.005 Gm. of "Natrium fluorat. puriss." Though I am not convinced of the efficacy of the method, I thought it justified to give it a trial in treatment of the patients with keloids in the Los Angeles County General Hospital. I shall report on the results, if any.

DR. KENDAL FROST: I wonder whether the concentration of fluorides in the blood has something to do with this lesion, because in some of the southwestern states, Colorado, Arizona and New Mexico, there are natural fluorides in the water, and children born in that part of the country have brown spots on their teeth. All the children born there and living there for the first few years of their life have discolored teeth.

DR. IRVING BANCROFT: I wanted to know particularly the time to apply the radiation. Should it be immediately after the incision or four to six weeks after? I should rather use irradiation and try the fluoride as suggested by Dr. Obermayer.

DR. KENDAL FROST: I do not know where I got this information, but I have the distinct impression that irradiation given at the time of operation or at any time before formation of the subsequent keloid is of no benefit. I have tried it on one or two patients, and it did not work when applied immediately after operation.

DR. STANLEY ANDERSON: In the treatment of such a thickened keloid my suggestion would be to excise the lesions and then give a fairly large dose of roentgen irradiation once weekly for four to six treatments at the first sign of a reappearance of keloidal tissue.

DR. H. C. L. LINDSAY: For many years I have understood that infinitesimally small amounts of hydrofluoric acid contained in some drinking water are injurious to teeth, especially to the enamel. Last year I read an article in the December issue of *Progress Digest* which stated that sodium fluoride may be used in large doses for the building up of the tooth structure. The normal fluorine content of wisdom teeth of a healthy adult is about 0.016 per cent. The concentration of fluorine in the water supply is apparently dangerous when it exceeds 0.9 part per million parts of water. Up to that point, according to Drs. J. F. McClendon and W. C. Foster, it seems to have a helpful influence in enabling the teeth to resist decomposition (*J. Dent. Research* **21**:139, 1942).

A Case for Diagnosis (Fibroma?). Presented by DR. SAMUEL AYRES JR.

B. S., an 18 year old white girl, has had tumors on two of her toes for two to three years. The larger lesion has been removed twice by "electric needle," the last time six months ago. Recurrence took place after each treatment. A smaller lesion has been present for about one year and has never been treated.

Two lesions are present. The larger is of approximately the size of a navy bean and is on the outer aspect of the first phalanx of the left third toe; it consists of a slightly erythematous fibrous nodule showing dilated capillaries. The other lesion is somewhat smaller and is located on the under surface of the right second toe in the medial portion. This lesion is similar in appearance except that it is more flesh colored. Both lesions have a somewhat translucent appearance. A specimen was taken for biopsy from the larger lesion.

I have not given any treatment. Biopsy showed hypertrophy of the corneous layer and an increase of fibrous tissue in the corium.

DISCUSSION

DR. KENNETH STOUT: I thought the lesions were probably intradermal fibromas.

DR. SAMUEL AYRES JR.: The lesions are rather insignificant, and yet, like so many insignificant things, they can bother one. Here is a girl with little lesions on her toes, one of which was removed twice and recurred and the other of which has been present for about a year. The two are identical. They are flesh colored, slight pink, and are obviously not warts. I thought only of some kind of fibroma, but I have never seen any lesions exactly like them.

DR. SAUL ROBINSON: I recall a lesion similar to the ulcerated lesion of a soft corn.

DR. SAMUEL AYRES JR.: That apparent ulceration was due to the removal of the specimen for biopsy. The lesion was not ulcerated.

A Case for Diagnosis (Xanthoma?). Presented by DR. NELSON PAUL ANDERSON.

L. L. A., a 42 year old white woman, first noticed an eruption on the left malar region in 1932. A few months later she noted a similar eruption in the right malar region. Between one and two years later she noted lesions on both sides of the neck and on the upper part of the chest.

She now presents ovoid to annular erythematous slightly raised plaques, one on each side of the neck. In each malar region and extending to the outer canthus of each eye, are two sharply marginated plaquelike lesions which have a distinct yellowish tinge along the upper margin and a definite pink to red color elsewhere. There is a peculiar reticulated erythema on the outer aspects of the arms. Actual cautery had been previously applied to part of the lesion on the left side of the neck.

DISCUSSION

DR. CLEMENT COUNTER: The evident diagnosis is xanthoma with the deposits of yellowish material one sees in xanthoma tuberosum multiplex. It is probably not xanthoma tuberosum, because it lacks the tuberous character.

DR. C. R. HALLORAN: In some of the involved areas there are parts in which there are xanthomatous deposits, especially those of the left cheek near the eye. However, many of the lesions certainly look clinically like lupus erythematosus, and others strongly suggest sarcoid. It would be interesting to perform biopsies on the various types of lesions.

DR. SAUL ROBINSON: I agree that there are xanthoma-like lesions here, but I do not think that the lesions belong entirely in the group of the xanthomas. It is possible that there are secondary lipoid changes. Together with xanthomatous changes, one sometimes finds cardiovascular degeneration. I noticed that this woman has had heart disease for some years.

DR. SAMUEL AYRES JR.: In view of the inflammatory aspects together with the xanthomatous change, I wonder if the disease could be an atypical form of xanthoma diabeticorum.

DR. W. H. GOECKERMAN: I do not believe it is possible to diagnose the disease clinically, but it is tempting to try to do so. I should not like to overlook lupus erythematosus, in spite of the yellow appearance of some of the lesions, because such a change of color could occur with lupus erythematosus. A biopsy should be performed.

DR. N. P. ANDERSON: Personally I thought these lesions were a most unusual type of xanthoma. My clinical diagnosis was xanthoma, but, not knowing much about the lesions, I did not classify it as to type. Incidentally, the blood cholesterol is normal. The patient has had a complete physical examination, and I assume that if she had sugar in the urine it would have been found. Clinically, she presents lesions that are the plaquelike types of xanthoma. I thought I could hear a "to and fro murmur" over the left side of the chest.

NOTE.—Biopsy showed xanthoma with definite fatty infiltration.

Lichen Planus Atrophicus. Presented by DR. SAMUEL AYRES JR.

M. H., a 59 year old white woman, has had hay fever and states that she had urticaria for fifteen years up to about one year ago, at which time she first noticed the present eruption, appearing on the back of her neck. (She is receiving treatment for angina pectoris.) Since then lesions have occurred elsewhere. Prior to coming here, the patient had had some kind of acid applied to different lesions without benefit.

She now shows lesions scattered over the arms, trunk, back of the neck and left thigh and knee. The most extensive lesions are on the flexor aspects of the wrists. All of the lesions are similar in appearance and consist of variously sized (approximately dime-sized to dollar-sized) areas showing a whitish rough atrophic lichenoid appearance. The centers of many of the lichenoid areas show tiny corneous plugs. On the dorsal aspects of the wrists the skin is rough and rather dry and presents a follicular hyperkeratosis.

DISCUSSION

DR. KENDAL FROST: This eruption seemed to me to be morphea rather than lichen planus atrophicus.

DR. W. H. GOECKERMAN: This whole group of papular lesions is extremely vague in actual nature. If I had to use a term for it, I should call it lichen sclerosus et atrophicus. I think that is a definite group and is not of the same nature as lichen planus. One practically never sees any evidence of lichen planus associated with lesions of this sort. The histologic structure is not the same. It may be preceded by the lichen albus of von Zumbusch.

DR. SAMUEL AYRES JR.: Every time a case like this one is presented, there is a difference of opinion as to which one of several closely similar diseases is present. I do not believe that the eruption is related to true lichen planus. I did not find any primary lesions that looked like lichen planus. On the dorsal aspects of the wrists there were definite roughening and hyperkeratosis. Whether what is called lichen atrophicus starts with such lesions and ends with an atrophy I do not know. I saw the patient for the first time yesterday. In view of the keratotic aspects on the dorsal part of her wrists, I gave her some vitamin A. I thought it might possibly prevent the eruption from spreading.

Lupus Erythematosus. Presented by DR. SAMUEL AYRES JR.

F. B. S., a 40 year old white man, states that his eruption began about eight months ago on the lobe of the left ear as a watery and crusted area. This had been treated as impetigo with 10 per cent ammoniated mercury ointment and seven doses of roentgen rays.

On his first visit, on Nov. 19, 1942, he stated that four days prior to coming in he was working in his garden while wearing an undershirt which was open in a "V" at the back of the neck, and was exposed to the sun. Two days later the eruption became much more irritated.

At that time the eruption was present on the upper part of the back, sharply limited by the V-shaped opening of his undershirt, and on the back and sides of the neck, behind the ears and on the ear lobes, and there was a slight eruption on the face, forehead and chest. The lesions consisted of ill defined erythematous and vesicular areas. The tonsils were inflamed and contained pus; they were removed about Dec. 4, 1942. In addition to this treatment, he has used local application of calamine lotion, a proprietary mixture of vitamins with iron and maganese by mouth and seven intramuscular injections of thio-bismol, 0.2 Gm. each.

The lesions have undergone some change and now show a somewhat irregular and slightly papular erythematous appearance. Some of the lesions, especially on the cheeks, are bright red. Those on the upper part of the back have a somewhat lichenoid appearance. Biopsy showed changes characteristic of lupus erythematosus.

DISCUSSION

DR. SAUL ROBINSON: I agree with the diagnosis, and I think that the interesting part of the eruption is the papular lesions on the dorsum of the neck.

DR. SAMUEL AYRES JR.: I think this case illustrates an unusual type of lupus erythematosus. When I first saw the patient, several months ago, he had been under the care of one of the members of this society with the diagnosis of impetigo. Many of the lesions were like impetigo but had ceased to look as much like it as previously. Many of them showed crusting and oozing. I could make no diagnosis at that time except that the patient was sensitive to light, as the lesions were on parts of the body exposed to the sun. Later the treatment progressed and the lesions changed their character, at one time they almost assumed a lichenoid appearance, but I think lupus erythematosus is probably a final answer. The lesions are much improved since the infected tonsils were removed.

Parapsoriasis. Presented by DR. H. C. L. LINDSAY.

B. E. E., a 30 year old Polish-American man, has had a nonpruritic papular eruption, worse in winter, for the past three years. The lesions, which are sparsely scattered over the body and penis, are small slightly pigmented papules which are for the most part smooth. Some are the size of a small pea and bear a white psoriasiform scale; the smooth flat-topped papules exhibit such a scale on scraping, but none present papillary bleeding points as seen in psoriasis. The patient has suffered from mild arthritis affecting the hands and feet during the past three years.

The Wassermann reaction was negative. A biopsy showed a rather thin epithelium and relatively few rete pegs. There was universal edema in the upper layers of the corium, and an occasional area of round cell infiltrate was found about some of the superficial blood vessels. The deeper tissue was not remarkable.

DISCUSSION

DR. ANKER JENSEN: I thought the lesions were psoriasis.

DR. SAUL ROBINSON: I thought that they belonged in the group of parapsoriasis, particularly parapsoriasis varioliformis. The duration is about five months, but in some of the cases the eruption continues for years. The patient happened to mention that some of the lesions had become necrotic and that there was ulceration in the central portion of them. I think that perhaps this eruption is a chronic form of parapsoriasis varioliformis.

DR. C. R. HALLORAN: Most of the lesions simulate a parapsoriasis. However, the lesions on the penis and on the flexures of the arms and legs strongly suggest lichen planus.

DR. SAMUEL AYRES JR.: I thought the eruption was pityriasis lichenoides varioliformis of the subacute type.

DR. N. P. ANDERSON: I think this patient presents a lichenoid type of parapsoriasis. I should like, if Dr. Lindsay can arrange it, to have dark adaptation tests done. I do not know of any one doing this work. This man gives a definite history of night blindness, and if it is ever going to be learned whether vitamin A does any good in parapsoriasis, this case offers a chance to investigate it. The patient's eyes are also sensitive to light.

Piedra. Presented by DR. NELSON PAUL ANDERSON.

(A microscopic slide of hair from a patient with piedra was shown.)

DISCUSSION

DR. M. E. OBERMAYER: Dr. Anderson has provided an opportunity to see a disease which is rarely encountered in the United States. Physicians are apt to confuse piedra with trichorrhexis nodosa. However, while in the latter disease the hair breaks off at the site of the nodosities, it remains unbroken in the former. Moreover, the nodules of piedra are smaller and firmer, though not as hard as the Spanish designation (stone) would suggest, and examination by the potassium hydroxide method reveals a mosaic of large spores of Trichosporum giganteum; fungi cannot be demonstrated in trichorrhexis nodosa.

DR. N. P. ANDERSON: I thought it would be worth while to present these hairs infected with piedra. I have not looked elsewhere than in the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY, but it seems that this is the first case of piedra presented in the United States. Incidentally, I encountered another case of the disease in a youngster about three years ago. He had been sent home from school on account of infestation with louse nits. The mother applied the delousing and denitting process, without much effect. Clinically the youngster had a decided involvement throughout the scalp. It was definitely determined microscopically that the boy had piedra. The hairs presented tonight are from a Mexican girl whose personal hygiene is above reproach. She has a few of the affected hairs in each temporal region. The stony concretions are close to the scalp, perhaps 1 cm. up on the hair.

Multiple Chancriform Lesions on the Penis. Presented by DR. H. C. L. LINDSAY.

Mr. C. H., a 49 year old white man, has had the present penile lesions for about a month. He now presents multiple lesions on the glans penis and prepuce, one of which is on the dorsum of the penis and is so indurated that when the prepuce is retracted one edge projects like the tarsus of an everted eyelid. Other lesions are small; some are punched out, and others are mere abrasions. Slight pain is present; no involvement of lymph nodes is detectable.

When he was first seen, two weeks ago, there was a nondescript transient rash on the abdomen (confined to the belt area) not suggestive of syphilis. Later, whitish scales developed which could be peeled off with difficulty on the lower lip. He has had no headache or other systemic symptoms.

The Frei reaction was mildly positive. Repeated dark field examinations have not shown Spirochaeta pallida. Stained smears have not shown spirochetes, but cultures have shown Staphylococcus aureus.

Before two weeks ago, bismuth–formic acid–iodide powder had been applied, but since that time local application of isotonic solution of sodium chloride has been the only treatment.

DISCUSSION

DR. IRVING BANCROFT: It seemed to me that this man has lichen planus. I have seen such lesions, perhaps not quite so extensive and with not so much of a rolled border, but the lesions in the mouth impressed me as being lichen planus.

DR. SAUL ROBINSON: I think that this man has a multiple chancroidal infection. It is often difficult to find the Ducrey organism. I recently had a patient who presented a similar picture. That particular patient had a positive cutaneous reaction to Ducrey bacillus vaccine.

DR. ANKER JENSEN: It was my impression that this could be lichen planus. There is a flat lesion with a shiny top on the end of the penis. Some of the others had the same characteristics. I agree that some are slightly ulcerated. Also, lichen planus is sometimes encountered with a vesicular type of lesion, and possibly this lesion is that type. The mucous membrane on the inside of the cheek was abnormal.

DR. M. E. OBERMAYER: Dr. Lindsay gave me the privilege of examining this patient four weeks ago. At that time I felt certain that the lesions were multiple hard chancres. Their induration and the location on opposing surfaces, their sharp demarcation and flat surfaces were textbook features; the absence of swelling of the regional lymph nodes, though uncommon, is encountered at times, and I thought that repeated dark field examination would eventually reveal the presence of S. pallida. Now that four more weeks have elapsed without confirmatory observations, I realize that the disease is not syphilis, but I have no diagnosis to offer. It is surely not lichen planus; I should hesitate to consider lichen planus in the diagnosis of lesions with eroded or ulcerated surfaces.

DR. KENDAL FROST: I can conceive of its being a late syphilid with a negative Wassermann reaction.

DR. SAMUEL AYRES JR.: I suggest a diagnosis of chancriform pyoderma. I have seen one or two such lesions on the penis which were difficult to differentiate from a chancre, although they do not show lymphadenitis, as does a chancre. This patient said that a month

ago he had an eruption on his body. He did not receive any treatment. I wondered if he had scabies, with resulting lesions on the penis, which became infected with a pyogenic infection.

DR. CLEMENT COUNTER: I do not think syphilis can be ruled out. The patient should have further serologic examinations.

DR. A. FLETCHER HALL: My first thought clinically was lichen planus, in spite of the "ulceration," which I was inclined to consider as an erosion following the rupture of a vesicle. I did not think it chancroid, and I do not believe that a diagnosis can be made without a biopsy of the penile lesions.

DR. H. C. L. LINDSAY: It was thought that by Wassermann tests repeated at intervals it could be determined whether syphilis was present. Herpes with secondary infection was considered but a diagnosis of lichen planus was not entertained on account of the deep ulceration. Expert pathologists were not able to find any causative germs except staphylococci (Staph. aureus). On one of the pieces of pellicle from the upper lip was found a diplococcus too big to be a gonococcus. This germ as yet has not been identified. The patient is steadily getting better, using nothing but isotonic solution of sodium chloride on the lesions.

NOTE.—This patient was presented at the April and May meetings, and his case was discussed further.

A Case for Diagnosis. Presented by DR. ANKER K. JENSEN.

A young white shipyard worker states that five years ago a small swelling appeared under his right nostril. The area never returned to normal, and since then the extent of the swelling has gradually increased. There has been no tenderness or soreness.

The patient now shows a doughy thickening of the upper lip, under the nose. No discrete nodule is felt. The skin over this area is erythematous, and there is some folliculitis; the superficial infection has cleared up, however.

The Wassermann reaction was negative. Eight roentgen treatments of 75 r each have been given, and oxyquinoline sulfate ointment has been used locally.

DISCUSSION

DR. NELSON PAUL ANDERSON: I think this lesion is an angioma. I do not know how to classify it otherwise. I suspect that at some time or other this man has received a blow from a fist, perhaps years ago, and that some damage to the blood vessels occurred. By looking closely in the right nostril, one finds a small angioma, possibly an angiolymphangioma, probably of traumatic origin.

DR. SAUL ROBINSON: I believe that if a biopsy were performed it might be of help in the diagnosis. The lesion may even be a sarcoid; on palpation it felt rubbery and firm.

DR. M. E. OBERMAYER: The elastic character of the swelling and its failure to pit on pressure favor the diagnosis of postinflammatory lymphedema or elephantiasis, with which the history of follicular pustulation at the onset is in accord.

DR. STANLEY ANDERSON: I thought the lesion was a lymphangioma with a degree of obstruction of the lymphatic vessels.

DR. W. H. GOECKERMAN: I am inclined to favor Dr. Nelson Paul Anderson's conception. When I first saw the swelling, I thought it was edema, but the consistency did not seem right to me. It is peculiarly doughy and pudgy. I think there is some real vascular abnormality.

DR. SAMUEL AYRES JR.: I questioned the patient as to whether any pustules were present, and he said that there were none. He said the lesion varies some in its elevation. At some times it is more inflammatory than at others. This would rule against its being an angioma or other vascular disease. A fixed eruption in that location would produce a certain amount of swelling. The patient admitted taking anacin occasionally. I think it would be a good thing to check on the possibility of a drug eruption.

DR. H. C. L. LINDSAY: The lesion of the lip simulates that seen in the cauliflower ears of wrestlers and boxers. Contusions result in faulty flow of lymph and blood, and a permanent swelling, a sort of elephantiasis, results.

DR. ANKER K. JENSEN: I was of the impression that this was a local lymphedema. If the patient will permit a biopsy, I will have one performed.

NOTE.—Although considerable bleeding was encountered at the time the biopsy specimen was removed and microscopic examination showed numerous new blood vessels, nothing of a definitely angiomatous nature was identified.

Book Reviews

Kozhniy leishmanioz (Cutaneous Leishmaniasis). By Prof. P. V. Kozhevnikov. Price, not given. Pp. 21. Ashkhabad: Dermatovenerologic Institute of Scientific Research of the People's Commissariat of Health of the Turkmenian Soviet Socialistic Republic, 1942. (In Russian.)

Cutaneous leishmaniasis is endemic in certain areas of the Soviet Union. The Russian physicians working there have the opportunity to study a great number of cases of this disease and make valuable observations. Some of these have been presented by Kozhevnikov in his pamphlet.

He describes two forms of cutaneous leishmaniasis: one with slow course and late ulceration and one with rapid course and early ulceration.

The first form is common in cities. Its incubation period is long, from three to twelve months. It begins as a roundish, somewhat elevated nodule, 3 to 5 mm. in diameter, with a smooth and shiny surface. In two to three months it becomes scaly or crusted. There is neither itching nor pain. In the third or fourth month the ulceration begins. The ulcer is first covered with a crust, which later falls off; there are then revealed a grayish or reddish base, elevated brownish red edges and a slightly purulent secretion. The size of the lesion varies. It may remain small or it may reach large dimensions, especially under the influence of trauma or other unfavorable conditions. The disease is fully developed in nine to twelve months after its beginning. The ulcer heals between the tenth and the eighteenth month, leaving a scar.

The second, early ulcerating, form of cutaneous leishmaniasis differs in its distribution, clinical picture and course from the aforementioned one. It is common in the suburbs or rural districts. The incubation period is short, from one to four weeks. The disease develops rapidly. Redness and swelling are followed in five to fifteen days by an ulcer around which satellite nodules may appear. The latter either undergo involution or turn into ulcerations. There is considerable pain. Lymphangitis may develop, with the formation of firm subcutaneous nodules which may ulcerate. Edema of the extremities, especially of the feet, may be observed. The disease reaches its full development during the third or fourth month. The ulcer heals in the fifth or sixth month, leaving a scar.

In both forms of the disease the number of lesions may vary from one to several dozens. The second form gives, in general, more numerous ulcers than the first. Any part of the skin may be affected. The face, the hands and the feet are mostly involved. In some cases the disease may last several years owing to the formation of new nodules on the edges of scars left from the primary ulcers. The picture then resembles lupus vulgaris ("lupoid leishmaniasis").

Cutaneous leishmaniasis leaves a permanent immunity. A second attack usually does not occur. However, persons who have had one type of the disease may later acquire the other type.

Leishmanias which cause the disease appear in the tissues as round bodies with two nuclei. They are not motile in the human body but exhibit flagella and motility in the body of the mosquito, which, according to Kozhevnikov, transmits the infection to man by its bite.

Cutaneous leishmaniasis is common in certain parts of the Soviet Union, namely, Turkmenia, Uzbekistan, Tadzhikistan and Transcaucasian Republics. In the rest of the country only occasional imported cases are observed. Only a few of many known species of mosquitoes can transmit the disease. In one locality where the second (early ulcerating) type of leishmaniasis was prevalent, only 3.5 per cent of all examined mosquitoes contained leishmanias. The number of infected mosquitoes was much less in the cities, where the first (late ulcerating) type of the disease is common. Certain observations suggested that in the city of Ashkhabad only 1 out of 2,000 mosquitoes was infected.

The wide distribution of the disease and its importance for the public health become clear from the statistics given by the author of the pamphlet. In Ashkhabad 15 per cent of school pupils who lived there only one year became infected. The same percentage contracted the disease during the second and third years of living there. All persons who had lived there ten years or longer, with a few exceptions, had the disease.

The fight against cutaneous leishmaniasis requires knowledge of the breeding places of mosquitoes. In the rural districts and suburbs of Turkmenia, a country with a dry climate, where the early ulcerating type of the disease is prevalent, mosquitoes breed in the holes of rodents. The latter also suffer from leishmaniasis. From 23 to 35 per cent of mosquitoes found in the holes contained leishmanias. In the cities, where the late ulcerating type of the disease is common, the breeding places of mosquitoes have not yet been determined. The holes of city rodents were found free from them, and the animals themselves were not infected.

The author describes an interesting experiment which proves the importance of the desert rodents and mosquitoes living with them as carriers of leishmaniasis. In one locality more than 500,000 holes of rodents in an area 1,250 hectares (1 hectare = 2.47 acres) were poisoned with chloropicrin, which killed the animals and the mosquitoes. Thereafter the number of new cases of cutaneous leishmaniasis per year dropped from 680 to 4. This procedure is rather expensive, and its effect lasts only one or two years. Then it must be repeated. In cities this method cannot be employed, and the measures must include improvement of sanitary conditions, extermination of rodents and infected dogs and destruction of mosquitoes in the dwellings by fumigation with the powder of pyrethrum (4.0 to 1 cubic meter for 1 hour). Spraying with "flicid" (an infusion of pyrethrum in kerosene) is also effective.

For personal protection against mosquitoes the author advises the following measures: (1) Covering the bed with a net during sleep; (2) protecting the entire room by use of gauze curtains in the windows, by closing of crevices in the walls, ceilings and window frames and by periodic fumigation with pyrethrum; (3) catching mosquitoes by sticky flypaper or plain heavy paper smeared with castor oil; (4) wearing nets protecting the face and neck (nets and curtains can be moistened with an aromatic substance repelling mosquitoes, such as saponated solution of cresol, turpentine or tar), and (5) painting the skin with oil of cloves to repel the insects.

Discussing the value of inoculation with cultures of Leishmania as a prophylactic measure against infection, the author states that this procedure is justified only for persons who expect to live for a long time in an infected locality. Under such circumstances they may expect sooner or later to contract the disease, which may develop in an especially unpleasant form of multiple ulcers or on the exposed parts of the body. A permanent immunity can be produced only by inoculation with cultures of living organisms grown on nutritive mediums. Dead cultures do not give immunity. Inoculation is usually made on the skin of the arm or of the thigh. The leishmanias causing the two types of the disease are biologically different. Those isolated from a lesion of a late ulcerating form on inoculation produce a lesion of the same form, which lasts about one year, and the immunity develops in twelve to fifteen months after the inoculation. Leishmanias obtained from the early ulcerating type produce a similar lesion lasting about six months and the immunity develops in seven to eight months after the inoculation. The immunologic specificity of both forms of cutaneous leishmaniasis has been proved by the fact that persons inoculated with one form may later acquire the other form. Therefore, the inoculation must be made with the type prevalent in a given locality; in cities with the first type and in rural districts with the second type. Persons who often travel from place to place can be inoculated with both types.

As far as the therapy of cutaneous leishmaniasis is concerned, the author states that in the late ulcerating form of the disease the most favorable time for treatment is the first one or two months, when there is only a nodule present. It can be completely destroyed and the entire process liquidated by injection of a 5 per cent solution of acrichine or by electrocoagulation. A hardly noticeable scar or even no scar at all is left. A rapid cure is still possible in some cases even after three to six months. However, if the disease has spread in depth and peripherally, it is impossible to destroy all organisms without much destruction of the tissues. In such cases the nodular lesion, covered with some ointment and protected from trauma, is left to its usual course. The more active treatment begins in the stage of ulceration, which can be limited and shortened.

The early ulcerating form is not amenable to an abortive treatment. Here the disease develops so rapidly that the patient appears usually with an ulceration. The average duration of treatment even of serious forms of acute ulcerating leishmaniasis is about twenty to thirty-five days under hospital conditions. The author remarks that fresh lesions require a more prolonged treatment, while those of longer standing yield faster. For external use the author advises ointments containing 10 per cent of acrichine, 5 per cent of protargol, 0.5 per cent of rivanol (2-ethoxy-6, 9-diaminoacridinium hydrochloride) or 10 per cent of sulfanilamide. For internal treatment preparations of sulfanilamide, acrichine and antimony are used.

Fundamentals of Immunology. By William C. Boyd, Ph.D. Price, $5.50. Pp. 446, with 45 illustrations. New York: Interscience Publishers, Inc., 1943.

This is a remarkably complete, lucid yet brief, exposition of many important phases of immunology. An idea of the scope of the work is given by the following list of chapters: Immunity and Immunology; Antibodies and Antibody Specificity; Antigens; Cell Antigens; Blood Groups; Antibody Antigen Reactions; Complement and Complement Fixation; Anaphylaxis and Allergy; Allergy and Immunity, Bacteria, Viruses, Parasites; Practical Use of Artificial Immunity; Laboratory and Clinical Technic.

Laboratory immunology is a difficult science for most beginners and is practically a closed book for many physicians, and certain phases of the subject are not easy for even the experienced laboratory and research man to grasp and to retain. Particularly meritorious in the present text are the precise, brief explanations of such subjects as the blood groups, the isoagglutinins and agglutinogens, the chemicophysical principles of antigen-antibody reactions, the technics of laboratory procedures and the mathematical bases for evaluating the significance of serologic and other immunologic results.

The clinical aspects of immunity and hypersensitivity are sketched in simply to round out the picture, with no pretense at clinical description or exhaustive discussion. It is perhaps unfortunate that the author could not omit the term "allergy" entirely from his text. Boyd gives his reasons for choosing to consider "allergy" as covering only specifically acquired hypersensitivity, and also his reasons for not hesitating to include phenomena of both immunity and destructive hypersensitivity under the heading of "immunology." Thus, for example, he points out and attempts to justify the paradox which exists in speaking of a rabbit or guinea pig which has been exposed to a foreign protein as "immunized" to that protein, even though the next contact with that protein will kill the animal.

Paradoxes of this sort are, of course, the inevitable consequence of failing to adopt some nonprejudicial term to cover all of the fundamentally related but outwardly divergent, specifically acquired alterations in the capacity of living tissues or organisms to react. Boyd correctly states that when Von Pirquet coined the word "allergy" his principal purpose was to supply a nonprejudicial term to cover specifically acquired changes of all sorts and thus to avoid the absurd paradoxes which are always sure to occur when no such inclusive term is available. In the opinion of the reviewer, if the word "allergy" is not employed for the purpose for which it was intended, it has little or no place in medical or scientific language and had best not be used at all. As Boyd points out, the popular usages of the word have robbed it of all precision.

On the whole, the author's choice of definitions as well as his selection and omission of subjects has been excellent and dictated by clear reasoning. This is a refreshing departure from that which is encountered in the majority of texts in this field. Boyd's book is undoubtedly the work of a learned student and stimulating teacher. The clarity and brevity of the presentations, the completeness of the exposition and the inclusive bibliographies should render this book invaluable to all clinicians and laboratory workers interested in the principles of immunology.

Methods of Diagnostic Bacteriology. By Isabelle G. Schaub, A.B., and M. Kathleen Foley, A.B. Second edition. Price, $3.50. Pp. 430. St. Louis: The C. V. Mosby Company, 1943.

To all intents and purposes, this is a cook book for the bacteriologic laboratory, for which there is a definite place. Plenty of blank pages are provided for the supplementary data that come freshly to hand in all laboratories. Data are comprehensive, complete and expressed in short form; perhaps the authors are sketchy in supplying the indications for the employment of tests, but, again, this may not be within the scope of such a book.

For the purposes of the dermatologist, the section on yeast and fungi is inadequate, consisting as it does of only seven pages. Perhaps there is an inaccuracy on page 87, where it is stated that "yeast and monilia are usually small, dry, chalky white and opaque"; surely they cannot be regarded as dry, and only questionably can they be said to be as chalky white. Again, on page 89 the statement appears that "colonies of fungi are usually fuzzy. . . ." Here the authors are probably referring to the saprophytic molds; the term "fungi" is widely inclusive indeed. Perhaps, too, information about Coccidioides immitis is justified, in view of its mounting importance in United States Army establishments in the Southwest (valley fever). All in all, though, the book is decidedly worth while and should serve as an almost indispensable elbow companion in a bacteriologic laboratory.

Dictionary of Bio-Chemistry and Related Subjects. Editor in chief, William Marias Malisoff, Professor of Biochemistry at the Polytechnic Institute of Brooklyn. Price, $7.50. Pp. 579. New York: Philosophical Library, Inc., 1943.

This book is a new departure in the "dictionary" field, combining features of both glossary and encyclopedia. What there is of it is good. In limiting this effort to less than six hundred pages, the editor in chief solved an unsolvable problem, what to omit and why. This type of dictionary should be encouraged.

The editor in chief and his collaborators are entitled to support in attempting a much larger dictionary.